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THE THALAMUS IN THE PHYSIOLOGY AND PATHOLOGY OF THE MIND*

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The rôle of the thalamus is one of the most interesting and most important problems. The thalamus is essentially the receptive or sensory portion of the primitive or segmental brain, the paleoencephalon. The relation it bears to the impacts which the organism receives from the outside world and to the transmission of these impacts to the neoencephalon, the cortex, gives it a significance and value altogether peculiar. Too often its importance is overlooked or, it may be, underestimated.

When we turn our attention to the cephalic end of the nervous axis of a simple vertebrate form, such as a fish, we note the presence of certain aggregations of neurons which stand in definite relation to certain receptors. The first aggregation is that constituting the olfactory lobe; this is in close relation with the olfactory mucous membrane. Back of the olfactory lobe we note a lobe related to the receptors in the eye; next an aggregation related to the receptors in the ear; and farther on other aggregations having equally definite relationships. Thus, in speaking of the dog-fish, Herrick says that we may recognize a "nose brain," an "eye brain," an "ear brain," a "visceral brain" and a "skin brain." Each brain is related to certain receptors and to these only. Each set of receptors and its corresponding nuclear aggregation is adapted to the reception of certain impacts or stimuli and to none other. Thus, the receptors and nuclear aggregations for smell can receive only the impacts giving rise to sensations of smell; those for sight, only the impacts giving rise to sensations of light; those for hearing, only the impacts giving rise to sensations of sound, and so on.

A brief consideration reveals the fact that one and the same object may furnish impacts for several different receptors. Thus, an object serving as food may be perceived by the fish through its odor; second, the object may be moving and thus throw impacts on the retina; third, in moving through the water it may produce sound waves and thus excite the organ of hearing, or possibly it may by producing coarse waves in the water excite the system of the lateral lines. Simultaneous,

* Read at the fortieth anniversary of the foundation of the Philadelphia Neurological Society, Nov. 28, 1924.

diverse, sense impressions are constantly and normally occurring, and in the more complex animal forms their number may be relatively large. Clearly, the correlation of such simultaneous impressions—their association with the same object, the object which is their common cause—is a matter of primal importance to the organism. In the fish, the reaction of the various nuclear aggregations receiving these diverse impacts is to discharge into the common paths concerned in swimming and in the ingestion of food. A real association of the changes induced in the various nuclear aggregations can hardly be said to exist. Obviously, the correlation of the diverse impacts would be greatly facilitated if these aggregations or their nuclear representatives could be grouped together in one structure; and this is what actually takes place in the thalamus. The thalamus has been happily termed the diencephalon or the between brain. In the higher animals of the vertebrate series, it lies literally between the midbrain (corpora quadrigemina and cerebral peduncles) and the telencephalon.[2]

Like the striatum, the thalamus presents an interesting and instructive history. Like the striatum, it is made up of an ancient and relatively recent portion; a paleothalamus and a neothalamus. Early, we find that fibers from the olfactory pathways join nuclear aggregations in the older portion—both in the part known as the epithalamus (in the habenula) and in the part known as the hypothalamus (in the eminences back of the optic decussation and in the mammillary bodies). These nuclear aggregations are in close relation with others that receive the impacts for taste and impacts from the viscera and from the body generally. In the newer portion of the thalamus, nuclear aggregations have made their appearance which are receiving stations in the pathways of touch, pain, temperature and other somatic sensations, together with the pathways of light and sound. These various nuclear aggregations are especially interesting, because in the course of evolution they have been advanced from lower levels in the segmental brain to the higher level of the thalamus and thus come into more immediate relation with the telencephalon; for instance, in the case of the pathways for the light impacts, the transition has been from the anterior quadrigeminal bodies which constitute the center—the final receiving station—for light in reptiles and birds, to the pulvinar and lateral geniculate bodies in the thalamus. Similarly, a transition from the ancient center for hearing in the posterior quadrigeminal bodies has taken place to the median geniculate body of the thalamus. The explanation of these transitions is doubtless to be sought in the principle of neurobiotaxis. Probably they took place gradually and in the forma-

2. In this article the term thalamus is used in the sense of the thalamencephalon and therefore embraces the epithalamus, the hypothalamus, the thalamus so-called and the metathalamus.

tive and embryonic periods of the ancestral forms. What was the attracting cause? Was it the closer and more intimate reactions brought about by that other newcomer, the telencephalon, or was it the presence of the other and older nuclear aggregations in the thalamus with which a constantly increasing interchange was taking place, and with which a closer biotactic relationship was brought about by movement into the thalamus? Probably both causes were at work. A dominating influence is apparently to be ascribed to the telencephalon, but the fact that most concerns us here is the grouping together in the thalamus, old and new, of nuclear aggregations in close relation with each other, which receive all of the incoming transmissions; all are, so to speak, assembled here.

What is the rôle that the thalamus plays in consciousness? Clearly, this rôle must be of great importance. Consciousness is of course inseparable from sensation. A separate sensation, however, such for instance as a mere ringing in the ears or a mere glow of light, can hardly give rise to a sense of existence. The same is probably true when the sensations are multiple if they remain unassociated. Even if associated sufficiently, as in fishes, to permit of responses along common paths, it is highly questionable whether the sensations result in anything more than a mere group of sensations—sensations that may or may not occur simultaneously. It is questionable whether such an arrangement can give rise to a sense of existence any more than a single and separate sensation. Certain it is that it cannot give birth to that community of consciousness which constitutes a "sense of self."

What is the result of the assembling of the nuclear aggregations in the thalamus, of assembling all of the impacts which the organism is capable of receiving? Setting aside, for the time being, their rôle of way stations in the pathways of transmission to the telencephalon, what rôle do they play in their relations with each other? In the first place, their close relation with each other must greatly facilitate responses along common paths; for instance, the close and primitive relations of the nuclear aggregations for smell, taste and the viscera must greatly facilitate responses involving, first, the intake of food and, secondly, the transmission of impulses along a common path to the digestive tract. Doubtless similar truths obtain in regard to the other nuclear aggregations and the transmission of impulses to other viscera; for example, to the circulatory apparatus or to the skeletal muscles or to various glands and other structures of the body. Such responses would make their exit by way of the motor structures in the subthalamus and the striatum. However, this integration and coordination of responses is not the only outcome of the assembling of the sensory nuclear aggregations in the thalamus. A result of far greater magnitude ensues. New sensations, new feelings are born, due not to impacts received

from without, but to impacts transmitted from the various nuclear aggregations to each other. Under given conditions, there is an "averaging" or "summation" of sensations. This may express itself negatively in a feeling of indifference or placidity, or it may express itself positively in a more or less pronounced feeling of comfort or sense of well-being. On the other hand, it may express itself in a feeling of discomfort, of distress, of suffering or of pain. Under given conditions, these sensations may assume a definite character; for instance, impacts transmitted from the digestive tract and from the body generally to the visceral and general somatic aggregations give rise to the sensations of hunger and thirst. An easy transition from these states results in a sensation of weakness and—certain factors being added—of fear. Under given conditions, as we shall see, the opposite emotion of courage, and it may be of anger, is experienced. It may indeed be safely claimed that the entire gamut of the sensations, feelings and emotions have their seat in the thalamus, and this is true alike of a simple sensation such as a touch or sound, of simple emotions such as like or dislike, love or hate, and of our most refined and sublimated esthetic experiences. To make the picture clear, however, and to place the facts in their proper perspective, an additional statement is necessary.

THE THALAMUS AND THE CORTEX

It will be recalled that the thalamus is in close relation with the cerebral cortex; indeed, all of its nuclear aggregations except the olfactory [3] are way stations in the pathways of transmission to the telencephalon. However, and this is most important, the direction of transmission is not only to the cortex but through the corticothalamic fibers away from the cortex and back to the thalamus. True to its intercallary function, the cortex transmits the impacts which it receives in many directions, and various combinations are formed among neurons receiving impacts from multiple and diverse sources. The exchange of impacts must be exceedingly complex and intricate, but in any event they must eventually resolve themselves into resultants of various kinds, which—owing among other causes to the great number, the dynamic mass, of the neurons of the telencephalon—overflow and are now transmitted in the reverse direction from the cortex to the thalamus. Here they have all the effect of new impacts; they now play on the nuclear aggregations of the thalamus in the production of "feelings" which correspond to the interplay of neurons in the cortex. That the latter share the "feelings" in a measure, is possible and probable, but their function is essentially synthetic, analytic, discriminative; the emotional reaction belongs to the thalamus. Synthesis results from the confluence

3. The olfactory lobes in mammalian forms have already established a direct connection with the telencephalon via the hippocampal gyrus.

of noninterfering impacts; analysis results from the fact that certain impacts having been admitted, others are automatically excluded, or are admitted separately as superimposed factors. In other words, if an impact which has been received is followed by a second in an opposite phase of motion, the second is neutralized; or, if it possess a new quality, the latter is admitted as a motion superimposed. The separation of impacts means analysis. The combined action of synthesis and analysis is necessarily discrimination.

In the interplay between the cortex and the thalamus one fact stands out with striking prominence, and that is the dominance of the cortex. This is evidenced in two ways. We have already seen that the train of transmission in the cortex possesses a relatively high dynamic level, and therefore whether new impacts transmitted by the thalamus find entrance depends on their intensity; it is purely a question of dynamics. However, up to a given point a certain degree of resistance is offered to new impacts by the train of transmission—the field of consciousness. Its neurons are, so to speak, already "saturated," and the synaptic resistance is raised. On the other hand, the higher dynamic level results, as we have already seen, in an actual return flow to the thalamus. At the thalamus the same thing occurs. Its neurons are already highly charged with incoming streams; synaptic resistance becomes established, and the activities of the neurons of the thalamus are lowered. In other words, an "inhibition" of the thalamus by the cortex obtains, and this inhibition is maintained to a greater or lesser degree in the normal condition of the organism. In diseased states notable departures are observed.

The facts in regard to the telencephalon and the thalamus may be briefly restated as follows: consciousness is the property of the neurons actually engaged in the train of transmission through the cortex. This is the "conscious field." Further, all consciousness is attended by "feeling," using this word generically to embrace the entire range of sensations; first, the special sensations received through the special receptors such as the sensations of touch, light or sound; second, various basic feelings such as hunger, thirst and the sexual feeling; third, various generalized feelings the result of the interaction of the nuclear aggregations of the thalamus among each other, such as comfort, discomfort, well-being, and various special feelings, such as fear and anger; lastly, more complex emotional states, the results of the interaction of the cortex with the thalamus.

Regarding the dominance, that is the inhibition, exercised by the cortex, there can be no question. This may show itself in regard to all of the feelings here outlined. As regards the special sensations, every one realizes that many purely physical impacts fail to gain entrance into the conscious field. A man busily engaged in writing does not hear

the clock ticking in his room; he does not hear the clock strike; indeed, he may be spoken to and yet no recognition by him of the fact obtains. What is true of sound is also true of other physical impressions of whatsoever character. It is also true of such basic feelings as hunger, thirst, pain, the sexual feeling. It is true likewise of the feelings of comfort, discomfort, well-being; true also of fear and anger; true also of the more complex emotions. Everything depends on what is going on in the cortex, on the interactions of its neurons, on the dynamic level of the conscious field. But this dominance has its limitations. If sound impacts are sufficiently intense and insistent, they force their way in. This is true also of hunger, thirst, the sexual feeling; the soldier who does not feel the pain of a wound during the excitement of battle, feels it later. The suppression of fear and anger likewise has its limitations, and this is true of all of our emotional experiences. It is, however, the dominance of the telencephalon that makes possible the coordinated adjustments favorable to the organism.

The basic importance of the thalamus in the physiology of mind lies in the fact that it is the seat of all the sensations, feelings and emotions which the organism is capable of experiencing. The extent to which these sensations are admitted to the train of consciousness in the cortex and the subsequent reaction of the cortex on the thalamus is, as we have seen, purely a question of dynamics. Under normal conditions, the interactions of the thalamus and cortex favor and lead to the safety, the success, the comfort, the pleasure and the happiness of the organism.

NUTRITION OF THE NEURON

Let us now turn our attention to another aspect of the subject. Other factors than the reception and transmission of impacts influence the behavior of the neuron. Among these are the nutritional and other agencies to which it is subject. The body of the neuron lies in a lymph space. As in the case of all other structures of the body, its relations to the blood stream are indirect; nutrition is effected only through the lymph in which it is immersed. This is, of course, equally true of the dendrites, axons and synapses; for the very capillaries that supply these structures themselves lie in lymph spaces. Contrary to the error frequently maintained, the lymph space in which the body of the neuron lies, the periganglionic lymph space, has no communication with the cavities containing the cerebrospinal fluid. The latter, as I have definitely shown,[4] is virtually a "common salt solution" which has the purely physical function of acting as a hydrostatic support to the

4. Dercum, F. X.: Functions of Cerebrospinal Fluid with Special Consideration of Spinal Drainage and of Intraspinal Injections of Arsphenaminized Serum, Arch. Neurol. & Psychiat. **3**:230 (March) 1920.

soft, mechanically vulnerable brain and cord. It has nothing to do with the nutrition of the nervous substance. The nutrition of the latter depends definitely and solely on its vascular supply.

The maintenance of the function of the nerve cell means the maintenance of its metabolism. The reception and transmission of impacts is accompanied by an electrochemical change. This change is one of reduction. Of necessity, it is attended by a consumption of substance, just as in the instance of the zinc plate of a galvanic battery. Hodge and others, years ago demonstrated a reduction in the volume of nerve cells as a result of the excessive exercise of their function. The loss is of course replaced by a corresponding upbuilding. The blood plasma transfers the necessary materials through the walls of the capillaries into the periganglionic lymph spaces; here they have ready access to the cell bodies. Under physiologic conditions, the catabolism and anabolism of the nerve cell go hand in hand; in other words, the materials for the electrochemical changes are supplied as fast as they are consumed. It is for this reason doubtless that normally nerve cells show no appreciable change as a result of their functional activity.

The nerve cells not only receive from the blood plasma the material necessary for their reconstruction, but are also exposed to other substances that profoundly influence their activity. Among these are especially the substances elaborated by the glands of internal secretion, the hormones.

SYMPATHETIC AND AUTONOMIC SYSTEMS

All the glands of internal secretion have to do with chemical changes. Some of them exercise a more or less general and widely distributed influence on the metabolism and nutrition of the organism; others are more or less special in their function, such as the sex glands, the cortex of the suprarenals and perhaps the pineal gland. Those whose action is more general resolve themselves into two groups whose effects on metabolism are diametrically opposed. The first consists of the thyroid, the pituitary and the chromaffin system; the second, of the thymus, the parathyroid and the pancreas.[5] These two groups stand in physiologic antagonism to each other. The thyroid, the pituitary and the chromaffin system form a synergic group; all of them increase metabolism, and all of them promote the release of energy. The thymus, the parathyroid and the pancreas form another synergic group. The pancreas and all the glands of the alimentary tract, together with its adnexa, are concerned with the processes of digestion and assimilation, i.e., with the storing up of energy. The thymus and the parathyroids are both in synergic relation with the pancreas and must therefore be

5. Dercum: Biology of the Internal Secretions, Philadelphia, W. B. Saunders Company, 1924.

included in this group. The close relations that exist between the chromaffin system and the sympathetic nervous system proper justify the application of the term sympathetic to the first group, while the vagotonic rôle of the thymus justifies the application of the term autonomic to the second.[6] The first is catabolic, the second anabolic in its action.

The readiness of response of the neuron is at times heightened, at times lessened, in accordance with the relative activities of the two groups. Under normal conditions, fluctuations occur within a comparatively limited range. For instance, during physical activity the sympathetic group—the chromaffin, thyroid, pituitary group—is dominant. An increase of function is noted in various organs; the muscles are intoned, the heart action is accelerated and strengthened, the respirations are increased in frequency, the pupils are dilated and admit more light. At the same time, the nervous responses are increased both in number and in volume; the organism is more alert and reacts more quickly. On the other hand, during periods of relative quiet, as for instance after the taking of food, it is the autonomic group that asserts itself. Digestion and assimilation are now dominant. The muscles are relaxed, the heart and respiration slowed. Nervous rest and quiet, perhaps torpor or sleep, ensue.

The question as to the mode of action of the internal secretions—the hormones—on the nervous system is exceedingly interesting. It is certain, for instance, that the thyroid secretion—or rather its active principle thyroxin—increases the intensiveness of the chemical processes going on in the body. The carbohydrates and fats reveal an increased metamorphosis. The consumption of oxygen and the output of carbon dioxid are increased, while the increase in the disintegration of the proteins leads to an increased output of nitrogen. The heightened activity of the neurons may be merely the outcome of the general increase of metabolism. However, the definite nervous symptoms observed in pathologic states in which the thyroid secretion is excessive—extreme restlessness, sleeplessness, active delirium—point to a direct action of the thyroxin on the neuron. It acts probably both on the cell-body by stimulating and perhaps modifying the metabolism of the latter, and also, in all probability, on the synapses, the action in the latter instance being to lessen synaptic resistance. Probably the action of the hormones of the chromaffin system and of the pituitary is both direct and indirect. Many of the nervous symptoms observed both in suprarenal and pituitary disease suggest a direct action; regarding the results of the action of the group as a whole, there can be no

6. Dercum: Footnote 3, pp. 59, 65 and 140.

question. The action of the autonomic group, the group concerned in digestion, assimilation and the storing up of energy, is likewise probably both direct and indirect. Direct action on the neurons is suggested by the lessening and slowing of the responses as though the metabolism of the cell-body were diminished and the synaptic resistance increased.

THALAMUS SEAT OF SENSATIONS

The fluctuations that occur between the activities of the two groups of the endocrins play an important rôle in the train of transmission through the cortex. At the time of the dominance of the thyroid, pituitary and suprarenal group—the catabolic group—both the speed and the volume of the train of transmission are increased; in other words, the individual thinks more actively and the field of his consciousness is enlarged. The reverse obtains when the autonomic group—the anabolic group—is dominant; thought is less active and the field of consciousness is contracted. In pathologic conditions, the fluctuations may be greatly exaggerated, and under such circumstances transmission is profoundly influenced; for example, in mania in which it is greatly increased in speed and volume, and in melancholia in which it is very greatly retarded and reduced.

Finally, and this is of special importance, the internal secretions play an additional and most important rôle in their action on the nuclear aggregations in the thalamus. In part this action is individual and specific, in part it is general and collective. It is exceedingly probable that in this way are excited the primitive sensations of hunger, thirst, fear and anger, and also the generalized feelings of comfort, contentment and well-being, or of discomfort and distress. These thalamic sensations, as we have already seen, serve as the basis for the more complex emotional states. Again, the hormone of the sex glands, by its action on the corresponding nuclear aggregation in the thalamus—in the floor of the hypothalamic portion of the paleothalamus—excites the sex feeling, the sexual want. All of these sensations, or rather the impacts into which they resolve themselves, find entrance under given conditions into the train of transmission in the cortex.

The Paranoid States.—The realization of the fact that sensations—feelings—may arise spontaneously in the thalamus as a result of the action of hormones or other substances circulating in the blood is of the utmost significance in the interpretation of the function of this important structure. It is safe to infer that as long as the substances circulating in the blood are normal to the organism, the sensations aroused in the thalamus are likewise normal, and that this is also true of the cortical reactions. However, it can be readily comprehended that when abnormal or toxic substances are present, given nuclear aggregations in the thalamus may be pathologically aroused and thus give rise to hallu-

cinations. Frequently the disturbance involves primarily nuclear aggregations which normally receive their stimuli from without, as in the case of the nuclear aggregations for the special senses, such as those for hearing or vision, or it may be those for taste or smell. Naturally, the impacts so arising when transmitted to the cortex are interpreted by the latter as things coming from without. They are referred to the external world, and we have here the birth of the delusions of reference. Frequently, the hallucinations are painful and distressing; at times intensely so. Of necessity they must give rise to combinations in the cortex that are painful; they cannot be pleasurable. What is more natural than that strange and disgusting hallucinations of taste and smell should give birth to the idea of being poisoned? Being poisoned, logically requires a poisoner. Again, painful auditory sensations, noises, cries and shrieks, sooner or later resolve themselves in the cortex into words, curses and abuse. Soon phrases and sentences are formed, soon they are attributed to various persons. Here we have the birth of the delusions of persecution so characteristic of the paranoid states.

The more acute hallucinatory disturbances noted in delirium and in confusion likewise find a ready explanation in the toxic action of infections and of poisons, primarily on the nuclear aggregations of the thalamus. The cortical reactions, as in the paranoid states, are always secondary.

Manic-Depressive Insanity.—In manic-depressive mental disease, however, there is a problem of peculiar interest. Unlike dementia praecox and paranoia, manic-depressive insanity is pictured neither by mental deterioration nor by the evidences of an incomplete and imperfect development. Its sole peculiarity consists in that the patient passes through wavelike periods of emotional depression, quiet and exhaustion, or, it may be, of emotional expansion and activity. At the conclusion of such a wavelike period, no impairment of the mental integrity of the patient is noted except in instances in which special factors have been at work. Frequently, waves of depression and expansion succeed each other, the patient passing through a cycle of the disturbance. In reality, the two phases constitute one clinical entity, to which the term manic-depressive insanity has come to be applied. Though presenting neither the evidences of an arrested development nor the history of mental deterioration, the affection is featured by a marked heredity. In 80 per cent. and more of the cases, a history of heredity can be elicited. What is it that is transmitted? What is the basic cause of the disturbance? As I have pointed out, this is clearly to be sought in the glands of the internal secretions.[7] As has been shown, the latter sepa-

7. Dercum: Biology of the Internal Secretions, Section XX.

rate themselves into two great groups: the autonomic and the sympathetic. The function of the first, let us repeat, is anabolic; it is concerned with the storing up of energy. The second is catabolic and is concerned with the expenditure of energy. In melancholia there is a great recession of function of the anabolic group; in consequence, melancholia is featured by nervous weakness and exhaustion, by atony and failure of the digestive tract, by reduction and feebleness of the circulation, by loss of weight and strength, and especially by mental depression. At the same time, we note that the expenditure of energy is reduced, at the height of the affection, to the lowest possible level. In other words, the group of glands innervated by the sympathetic—the chromaffin system, the thyroid and the pituitary—are also reduced in function. A diminished storing up of energy must inevitably be followed by a diminished output. Doubtless their lessened activity is also to be ascribed to an accompanying diminution of the sympathetic innervation.

After many months of quiet, rest and food, energy is slowly and gradually regained, and the normal level of metabolism is again reached. Unfortunately, the anabolic changes do not, in a large number of cases, stop here, but with increasing impetus sweep beyond the normal line; the sympathetic group becomes excessively active, and restlessness and expansion now replace the previous depression.

Melancholia.—Certain facts in regard to the mental symptoms must be noted. The depression that accompanies the recession of function of the autonomic group in melancholia is not only physical but mental. Indeed, as already stated, the characteristic feature of melancholia is the emotional depression. This emotional depression assumes the form of mental suffering, of mental pain. The feeling is akin to that which persons, otherwise normal, experience when subjected to sorrow and grief. The emotional pain of melancholia is clearly to be referred to the thalamus. The latter, as we have learned, contains nuclear aggregations which receive impacts from the various interoceptors and proprioceptors of the body. Under normal conditions, the sum total and averaging of these impacts gives rise to a sense of well-being. However, in melancholia, the impacts received from the organs concerned in reconstruction and the maintenance of energy—the impacts from the digestive tract with its important group of associated organs, from the heart and blood vessels, and from the various glands concerned in the anabolic processes—must be greatly changed both in their amount and in their character. That the resultant feeling aroused in the thalamus should depart widely from that in health, that instead of being pleasurable it should be distressing and painful, is readily comprehended. Further, it is exceedingly probable that the nuclear aggregations suffer in addition from an impaired nutrition and toxicity.

Another interesting reaction is now noted. It will be recalled that in paranoid states the patient refers his distressing thalamic sensations to the outside world and develops delusions of reference, delusions of injury, delusions of conspiracy. In melancholia, the exact opposite occurs. The patient refers the painful sensations to himself and develops ideas of self-blame, self-accusation and, finally, the delusion of the unpardonable sin. The following explanation of this reference to the "self" of the patient suggests itself.

In the first place, the impacts that enter the nuclear aggregations of the viscera and soma under normal conditions give rise to transmissions into the field of cortical activity which merely convey a vague and generalized sense of contentment, satisfaction and well-being. The train of transmission in the cortex is filled mainly with impacts received from the various exteroceptors of the special senses, i. e., the field of consciousness is dealing mainly with the outside world; impacts from the soma normally enter it in but slight degree. However, when the somatic nuclear aggregations are abnormally aroused, or when their activities are perverted, they force their way into the field of consciousness in greater degree. They are now "hallucinatory," but being interoceptive and proprioceptive in origin, they cannot be referred to the outside world; necessarily, they must be referred by the communal consciousness to itself. Some of the impacts received from the somatic nuclear aggregations are comparatively definite in character and lead to hypochondriac sensations referred to this or that part of the body, this or that organ. Thus arise the various "visceral hallucinations." Hypochondriac sensations, visceral hallucinations, enter into the symptomatology of melancholia in varying degree; sometimes slightly, sometimes largely. Especially is this likely to be the case in the melancholias of middle life. However, it is not a sense of the disturbed condition of the body that forms the characteristic feature of melancholia, but the presence of a painful emotion comparable to sorrow or grief which may reach the height of poignant anguish. The rôle of the thalamus in the "feelings," the emotions, has already been pointed out, and there is no good reason for regarding the emotional pain of melancholia as other than a disturbance of the nuclear aggregations of the thalamus and as hallucinatory in character. This is proved—one might almost say—by the existence of cases of melancholia without any other mental symptom than this emotional pain. In such cases, the patients make no reference of the pain to themselves, offer no explanations, develop no delusions. They simply suffer, sometimes horribly; they moan, perhaps cry out; sometimes rush to and fro; sometimes have outbursts of frenzy. When induced to answer questions, these persons are entirely lucid. It is this condition which is spoken of as lucid melancholia and by the older writers as melancholia sine delirio.

However, in the ordinary case of melancholia, as just pointed out, the patient refers the symptom to himself. He himself, and not some one in the outside world, is the cause of his suffering. A sense of wickedness, of guilt, naturally follows; and soon the cortex, utilizing some incident in the past life, usually trivial and often wholly imaginary, develops ideas of self-accusation and, finally, the delusion of the unpardonable sin.

Further, in some cases of melancholia special sense hallucinations are added; that is, the special sense nuclear aggregations of the thalamus also become involved. As before, these hallucinations are painful, and naturally in keeping with the exteroceptive character of the nuclear aggregations, they are referred to the outside world. They may consist of shrieks and cries, of scoldings, threats, vituperations, of tortures, burnings, horrible visions. However, they are regarded by the patient as punitive, as deserved, as only in keeping with the sins, the crimes he has committed; and thus they reenforce the self-accusations, the delusion of the unpardonable sin.

Another fact of importance must now be added; namely, that in melancholia there is a marked slowing, a marked retardation of the mental processes. Commonly, the patient answers questions slowly and only after an interval. Sometimes this symptom is exceedingly marked, the patient sitting as though spell-bound, answering with difficulty, uttering a few poorly enunciated words or perhaps not answering at all. There is clearly a delay of transmission which is to be referred not only to the depression of function of the cell bodies, but more especially to interference at the synapses, and this is entirely in keeping with the view that the depression of endocrine function is accompanied by a toxic action.

Mania.—In the phase of mania, on the other hand, the resistance of the synapses is greatly diminished; there is a general release of inhibition. The expansion and the enormously increased association of mania is in keeping with a heightened nervous outflow, the increased energy discharged by the neurons. Accompanying this are the motor excitement and the unusual, the bizarre, the pathologic character of the associations. We can understand, perhaps, why the nervous overflow should pass along unaccustomed channels; perhaps also, why the associations lose their intimate, elaborate and finer qualities, why they should become coarse or relatively so. Normal acts require time, probably in proportion to the amount of detail. In mania the discharges appear to be diffused en masse, probably along the larger pathways in which the least resistance is encountered. Possibly, there is here an explanation of the coarseness and superficiality of the associations. Finally, it is probable that fatigue early impairs the synapses on which the finer

adjustments depend, so that as the case progresses, coarse and flaring associations alone are possible.

Hallucinations and delusions are noticeably absent. Impacts stream through the nuclear aggregations of the thalamus to the cortex, but the sensations transmitted are not retained, not elaborated. The transmissions stream in massive volumes through the cortex to the motor exits. Only now and then and only during a temporary lull in the excitement does the patient behave as though he experienced hallucinations.

COMMENT

In summing up this brief consideration of the rôle of the thalamus in the physiology and pathology of mind, it may be well to point out that while in the interaction of the thalamus and cortex, the cortex is normally dominant, the thalamus controls the gateways of admission and in diseased states may hold the cortex at its mercy.

Finally, it should be added that there is one function of the thalamus which has not been touched on here. While the nuclear aggregations of the thalamus are undoubtedly influenced by the internal secretions, the thalamus in its turn contains centers which profoundly influence metabolism. These centers are situated in the floor of the hypothalamus and are probably in close relation with the visceral nuclear aggregations and have to do with the reactions of the latter on each other. That the resulting emissive streams should in turn influence the activities of the viscera and among these especially the glands concerned in anabolic and catabolic changes, is perhaps what we should naturally be led to expect.

CEREBROSPINAL FLUID FROM DIFFERENT LOCI*

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It is still an exceptional opportunity that makes possible the examination of cerebrospinal fluid obtained elsewhere than from the lumbar sac. While there are physicians who still look on lumbar puncture as an exceptional procedure, there are few who will not consider an examination of fluid at some other locus of the cerebrospinal system as extraordinary and unwarranted. Therefore our knowledge of fluid pathology in different parts of the ventricular-subarachnoid spaces advances slowly, and our conceptions of normalcy in these hidden regions becomes in a way a by-product of pathology. It should be emphasized here that in the case of an ambient fluid, postmortem study is of limited value and sometimes misleading.

Certain spaces in the ventricular-subarachnoid fluid system have been tapped sufficiently often to warrant an estimate of normal conditions at these loci, and to present in a number of pathologic states abnormal findings consistent enough to suggest their diagnostic or therapeutic worth. However, the whole subject of multilocular fluid examination must be considered as in a formative state, and open to constant revision.

The loci, other than the lumbar sac, which are now tapped without too great hesitation, are the lateral ventricles and the cisterna magna, and from examination of the fluid obtained from these three places most of the following conclusions are derived. Other loci, less frequently investigated, are the cerebral subarachnoid spaces, the cisterna chiasmatis, by means of Beriel's[1] orbital puncture, and the cervical and thoracic spinal subarachnoid spaces. Information of value may be obtained by a single puncture at any of these loci, but synchronous punctures at two or more loci are usually found to be much more valuable. Particularly are combined ventricular-lumbar, cisternal-lumbar and double lumbar punctures carried out without difficulty.

NORMAL FLUID IN VENTRICLE, CISTERNA MAGNA AND LUMBAR SAC

Judging from our records, we believe that the following represent normal relations in these three loci: The pressure is similar in all,

*From the Massachusetts General Hospital and Boston Psychopathic Hospital.

1. Beriel, L.: La ponction des espaces sousarchmoidiens cerebraux par la fente sphenoidale, Lyon Chir. **2**:320, 1919.

i. e., the height of the fluid columns in the manometers is on the same horizontal plane; the fluids are uniformly clear and colorless and do not clot; cells are absent in the ventricle, but frequently a few are found in cisternal and lumbar fluids under what must be considered normal condition. The Wassermann, colloidal gold chlorid, benzoin and mastic tests are uniformly negative.

While globulin (ammonium sulphate ring test) is normally absent in all three loci, slight but constant differences are seen in total protein content as indicated by trichloracetic acid and sulphosalicylic acid tests, the greatest amount appearing in lumbar fluid, less in cisternal fluid and least in ventricular fluid. While normal figures vary, 30 mg. per hundred cubic centimeters in lumbar fluid, 25 c.c. in cisternal fluid, and 10 c.c. in ventricular fluid would be considered as the normal ratio. Conspicuous is the opposite ratio in regard to sugar content. Sugar is greatest in amount in the ventricular fluid (approximately 0.08 per cent.) and least in the lumbar sac (average about 0.06 per cent.), with the cisternal fluid showing a value between these two. Insufficient data are at hand concerning normal values of fluid at other loci.

FLUID FROM DIFFERENT LOCI IN PATHOLOGIC CONDITIONS

Discussion may most profitably be centered on the results of examinations in syphilis of the nervous system, brain tumor, cerebral hemorrhage, meningitis, spinal subarachnoid block and tumors of the cauda equina.

Syphilis of the Central Nervous System.—In general paralysis, the fluids from the cistern and lumbar regions are practically identical, that is, we have never seen a fluid giving pathologic reactions from the lumbar sac which did not give similar reactions from the cistern, with the exception of those cases in which there was a block, nor have we found a positive cistern fluid with a negative spinal fluid. It has been noted at times that there is a slight difference in the cell count and in the total protein. However, this difference is relatively slight. There may be a few more cells in the lumbar fluid than in the cistern fluid, or the protein content may be a bit higher in the lumbar fluid. Aside from these minor differences, the fluids are the same. On the contrary, there is often a considerable discrepancy between the findings in the ventricular fluid and in the spinal or cisternal fluid, as shown in Table 1.

In cases of general paralysis in which the spinal and cistern fluids give a typical paretic reaction, the ventricular fluid may be normal, or there may be one or several pathologic reactions, varying however, in intensity from the reactions obtained in the spinal fluid. This may be true when a number of examinations are made at intervals. Thus, in the case of H. P., a typical paretic patient, we find on four separate ventricular

fluid examinations made in a period of two and a half months, that the Wassermann reaction was always negative with 1 c.c. of fluid. There was just a trace of globulin and possibly the slightest increase in total protein. The cells varied from 0 to 7. The gold reaction in all four tests gave a paretic curve. In the spinal fluid examination, the Wassermann test was always strongly positive. Globulin and albumin were markedly increased. The cell counts varied as follows: 18, 27, 39, 32.

TABLE 1.—*Comparative Examinations of Fluid from the Ventricle and from the Lumbar Sac in General Paralysis*

	Wassermann Reaction	Cells	Globulin	Total Protein	Colloidal Gold Test	Remarks
C. Mac.						
Lumbar.....	Pos. 0.05 c.c.	45	+	++	5555554220	No clinical improvement
Ventricle.....	Neg. 1.0 c.c.	30	0	Normal	5531100000	
Lumbar.....	Pos. 0.05 c.c.	14	++	++	3332220000	
Ventricle.....	Neg. 1.0 c.c.	2	+	+	0012200000	
Lumbar.....	Pos. 0.05 c.c.	10	+	+	5543332100	
Ventricle.....	Neg. 1.0 c.c.	6	0	Normal	5432100000	
S. G.						
Lumbar.....	Pos. 0.8 c.c.*	2	+	+	4443332220	No clinical improvement
Ventricle.....	Neg. 1.0 c.c.	2	0	Normal	1233321000	
R. C.						
Lumbar.....	Pos. 0.05 c.c.	..	..	..	5555431000	No clinical or serologic improvement
Ventricle.....	Pos. 0.8 c.c.	..	..	..	5431000000	
A. G.						
Lumbar.....	Pos. 0.2 c.c.	2	++	+	5555543100	Clinical and serologic recovery of 4¼ years' duration
Ventricle.....	Neg. 1.0 c.c.	0	0	Normal	0000000000	
A. F.						
Lumbar.....	Pos. 0.3 c.c.	0	++	+	4444221000	Clinical and serologic recovery; clinical recovery lasted more than seven years
Ventricle.....	Pos. 0.3 c.c.	1	+	+	4443221000	
Lumbar.....	Pos. 0.1 c.c.	5	+++	++	5555553300	
Ventricle.....	Pos. 0.1 c.c.	3	+	+	5555533000	
Lumbar.....	Pos. 0.3 c.c.	6	++	++	5555321000	
Ventricle.....	Pos. 0.3 c.c.	0	+	+	5532210000	
H. P.						
Lumbar.....	Pos. 0.6 c.c.	18	++	+++	5555544330	A good clinical remission was obtained and the spinal fluid made nearly negative; treatment stopped; clinical and serologic relapse and death
Ventricle.....	Neg. 1.0 c.c.	2	+	+	5543200000	
Lumbar.....	Pos. 0.2 c.c.	27	++	++	5555555542	
Ventricle.....	Neg. 1.0 c.c.	7	+	Normal	5555542000	
Lumbar.....	Pos. 0.2 c.c.	39	+++	+++	5555532100	
Ventricle.....	Neg. 1.0 c.c.	0	±	+	5555321000	
Lumbar.....	Pos. 0.2 c.c.	32	++++	++++	5555556210	
Ventricle.....	Neg. 1.0 c.c.	2	0	Normal	5552100000	
Lumbar.....	Positive	15	++	+++	5554430000	
Cistern.....	Positive	18	++	+++	5554433200	

* Considerable treatment preceded these tests taken at the time of the first ventricular injection.

The gold test always gave a strong paretic curve, much stronger than in the ventricular fluid. Subsequent comparison of the cistern and lumbar fluid from this case always showed practically identical reactions.

In another case, the ventricular fluid gave a positive Wassermann reaction, as did the spinal fluid. There were 9 cells in the ventricular fluid and 8 in the spinal fluid; there was no globulin, a normal amount of albumin and a negative gold reaction in the ventricular fluid, contrasted with increased globulin and albumin and a strong paretic gold curve (5555530000) in the lumbar fluid.

Similarly with patients undergoing treatment, the changes in fluid content, apparently dependent on therapy, do not run parallel in the ventricular and spinal fluids; in our experience, the spinal fluid is always stronger than the ventricular fluid. Changes occur in the ventricular fluid from one time to another, just as they do in the spinal fluid; the ventricular fluid may be weak on one examination and on the next one strong or weaker. However, there need be no correspondence between the changes occurring in the ventricular and spinal fluids. We have not been able to draw any clinical conclusions as to the course or prognosis of the case from the characteristics of the ventricular fluid; that is, the cases with a strongly positive ventricular fluid do not seem to have a different course than do the cases with a negative ventricular fluid.

TABLE 2.—*Acute Syphilitic Meningitis*

	Point of Puncture	Color, etc.	Cells	Protein, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.	Wassermann Test	Colloidal Gold Test
Mr. P., 21 years							
Before treatment ...	Lumbar	Opalescent, slightly yellow	1,500	236	34	Pos.	.....
Next day, 21 c.c. Swift-Ellis serum by lumbar puncture 18 hrs. before	Right lateral ventricle	Slightly turbid, slightly yellow, fine clot	1,246	81	54	Pos.	4433554311
Next day, 21 c.c. Swift-Ellis serum by lumbar puncture 18 hrs. before	Lumbar	Turbid, slightly yellow, large clot	1,460	400	30	Pos.	3444445532
Mr. R., 23 years							
Meningeal symptoms 3 wks.; primary 8 mos. (?) ago	Right ventricle	Cloudy, small clot	750	285	..	Neg.	5555554322
	Lumbar	Cloudy, fine clot	.....	857	..	Pos.	5555555321
Mr. H. Recent meningeal symptoms with choked disks	Ventricle	Cloudy	50	154	..	Pos.	2222111000
	Lumbar	Cloudy	174	237	..	Pos.	5555555321

In this connection it is interesting to note that Weigeldt [2] finds no such abnormalities in the ventricular fluids of five paretic patients, but he does occasionally find a positive Wassermann reaction.

Acute syphilitic meningitis is not a common type of syphilitic affection. However, in three such cases we have adequate evidence to show that as in the chronic form of neurosyphilis, general paralysis, involvement of the ventricle is not uncommon, although the evidence of a pathologic condition is less striking than in the cisterna or lumbar sac (Table 2).

It appears from the foregoing tables that these two types of neurosyphilis, primarily cerebral affections, frequently show abnormal findings in all three loci, differing only in intensity, but that the pathologic

2. Weigeldt, W.: Studien zur Physiologie und Pathologie des Liquor Cerebrospinalis, Jena, 1923.

process is uniformly more marked in the subarachnoid space than in the ventricles.

Meningovascular Syphilis, Spinal Type: A number of interesting points are brought out by a study of this group. All patients were submitted to combined puncture, because the possibility of spinal subarachnoid block was suggested by the clinical findings. Block was demonstrated in four cases, and laminectomy was performed in three. Two of these showed syphilitic lesions as the cause of the block. In Case 4 the block disappeared following antisyphilitic treatment (Table 3).

TABLE 3.—*Cases of Late Syphilis of the Nervous System in Which Spinal Subarachnoid Block Was Demonstrated by Manometric Studies*

Case	Color	Cells	Protein, Mg. per 100 C.c.	Wassermann Test	Colloidal Gold Test
1. Cervical hypertrophic meningitis:*					
Cisterna magna	Colorless	0	68	Neg.	.....
Lumbar sac	Clear yellow	6	800	Neg.†	001221000
2. Latent syphilis arachnoid fibroma:*					
Cisterna magna	Colorless	..	35	+	0455555655
Lumbar sac	Clear yellow	14	700	Anticomp.	0004556555
3. Gumma of spinal cord:*					
Cisterna magna	Colorless	28	68	Neg.	0014211000
Lumbar sac	Colorless	8	178	Neg.†	0002341000
4. Syphilitic meningitis:					
Cisterna magna	Colorless	6	42	+	0000000000
Lumbar sac	Clear lemon	24	90	+	0000112100

* Diagnosis confirmed by operation.
† Previously positive.

TABLE 4.—*Cases of Late Spinal Syphilis Presenting Transverse Myelitic Symptoms. Spinal Fluid Pathway Proved Open by Manometric Studies*

Case	Color	Cells	Protein, Mg. per 100 C.c.	Wassermann Test	Sugar-per Cent.	Colloidal Gold Test
5. Cisterna magna....	Colorless	0	26	+	.....	.....
Lumbar sac.....	Colorless	0	44	+	.....	.....
6. Cisterna magna....	Colorless	44	130	+	.....	5555541000
Lumbar sac.....	Colorless	40	150	+	.....	5555554311
7. Cisterna magna....	Colorless	100	67	+	0.054	0012210000
Lumbar sac.....	Colorless	120	138	+	0.055	0001333000
8. Cisterna magna....	.....	23	34	+	.....	0000000000
Lumbar sac.....	.....	72	43	+	.....	0000000000

Case 2 is of special interest because the cause of the block, an arachnoid fibroma, was found and removed. Subsequently, the block having been removed, the fluid findings were still characteristic of syphilis—strong evidence that we are here dealing with two entirely different pathologic conditions.

When block did not exist, syphilis of this type was found to yield almost similar findings in the cisterna magna and lumbar fluids (Table 4).

A third point of interest is the xanthochromia. In only one case of this series does a yellow color appear without block. However, we have seen numerous lumbar fluids from undoubted syphilitic cases of this character without evidence of cord compression or compressive myelitis.

It is, therefore, evident that combined punctures are of great help in the proper diagnosis of meningovascular syphilis in which there are transverse myelitis symptoms.

TABLE 5.—*Xanthochromia and Increased Protein Diminishing the Higher the Fluid is Examined, Suggesting Cauda Tumor* *

Tumor Found at Operation	Point of Puncture	Color, etc.	Cells	Protein, Mg. per 100 C.c.	Sugar	Wassermann Test	Colloidal Gold Test
J. M.: Tumor of cauda equina found at operation; extended upward to L2 vertebra	Cisterna	Light yellow, slight clot	0	174	58	Neg.	0223443000
	T12/L1	Dark yellow, slight clot	2	700	62	Neg.	0122474320
LaR.: Tumor, intradural, opposite L2 vertebra, Sept. 27...	L3/4	Deep yellow clot	Rare	2187	..	.....	.....
Oct. 6, at op.....	T3 level	Pale yellow, no clot	..	286	..	Neg.	.....
Oct. 6, at op.....	T12/L1	Lemon, no clot	..	720	..	Neg.	.....
No Lesion of Cauda Found at Operation							
A. B.: Symptoms suggest tumor of cauda equina							
Sept. 4.....	Cisterna	.....	4	95	..	.....	5554332100
Sept. 18.....	T12/L1	Slightly yellow, clot	11	213	75	(Neg. previously)	.....
Sept. 18.....	L2/3	Slightly yellow, clot	10	249	70	.....	.....
J. B.: Symptoms suggest tumor of cauda equina	Cisterna	Clear fluid, yellow	..	Slightly positive	..	.....	.....
Operation; no pathologic lesion of cauda equina	Lumbar	Clear fluid, yellow	..	Moderately positive	..	.....	.....
O. L.: Symptoms suggest tumor of cauda equina; no tumor found	Upper L	Colorless, clot +	3	126	65	Neg.	.....
	Lower L	Colorless, clot +	..	210	60	Neg.	.....

* This finding is not pathognomonic.

Cerebral Hemorrhage.—Weigeldt states that in twenty-two cases in which the subarachnoid spaces of the brain or spinal cord showed considerable amounts of blood at necropsy, the ventricles were found to be free from blood coloring matter and even erythrocytes. In only two cases was there slight blood contamination of the ventricle from hemorrhage at the base of the brain. This has been our experience in a limited number of cases. We have seen an equal amount of blood in the cisterna magna and lumbar sac shortly after cerebral hemorrhage, and an equal amount of xanthochromia in later stages. In determining the significance of the xanthochromia in such cases, we have found that

when due to hemorrhage, the color is the same, and the protein in both of these loci is approximately equal and only moderately increased in amount; whereas the xanthochromic fluid sometimes found above cord tumors, even as high as the cisterna, is less marked in depth of color and much less in protein content when contrasted with the lumbar fluid.

In hemorrhage into the ventricle there is little difference in the appearance of ventricular, cisternal and lumbar fluids.

Brain Tumor.—It is said by some authors that there are characteristic findings, particularly the colloidal gold curve, in brain tumor. We have not been able to demonstrate any abnormality of the lumbar fluid in some cases, and no consistent colloidal gold in others. We have found that the lumbar fluid usually contains an increased amount of protein, most frequently about twice the normal amount, but sometimes much more. Many authors agree with us in this finding.

In an effort to determine the point at which protein enters the fluid, as a possible aid in localization, a group of patients with brain tumor have been subjected to ventricular-lumbar puncture by our colleagues, Drs. Fremont-Smith and Hodgson. Their preliminary conclusions are that subtentorial tumors are accompanied by high protein occurring solely in the subarachnoid space, the ventricular fluid remaining normal; that tumors of the cerebral cortex frequently give rise to slight increase in subarachnoid protein, and that tumors in proximity to the ventricles cause an hyperalbuminous condition of the ventricular fluid which also appears in the fluid from lumbar puncture.

Acute Meningitis.—There is much difference of opinion concerning the findings in the acute forms of meningitides, those presumably of hematogenous origin, in which the meningococcus, pneumococcus and streptococcus are chiefly found.

Certain facts appear to be well founded:

(*a*) It seems certain that irrespective of the point of entrance of the organism into the meninges, the subarachnoid fluid, whether taken at the cisterna or lumbar sac, early in the disease shows a similar picture, that is, leukocytes and organisms with only slight increase in protein. The amount of fluid obtainable is increased.

(*b*) Later in the course of infection, perhaps by the seventh day, as the exudate increases in amount, there is a tendency for pus to gather at certain foci in the anterior basal cisterns and in the spinal meninges. It now becomes more difficult to obtain fluid by lumbar puncture. The examination shows enormous numbers of cells, chiefly polymorphonuclear leukocytes, but organisms are less numerous, and cultures may fail to grow. If at this stage the cisterna magna is tapped, a cloudy fluid is obtained showing fewer cells than in the lumbar sac and also less protein but a larger number of living organisms. If the ventricular

fluid is examined, it will often show an enormous number of organisms, but few cells.

(*c*) Somewhat later in the infection it frequently becomes impossible to obtain by lumbar puncture more than a few drops of fluid containing pus. The protein and cell count is still higher than before, the sugar has been reduced to 0, but no living organisms appear. A blocking of the meningitic fluid pathways is now apparent. The ventricle contains living bacteria.

The foregoing statements may be said to fairly summarize the impressions conveyed in numerous papers on this subject, and is in agreement with a limited personal knowledge of meningitic fluids. As a corollary to this conception, the introduction of curative serums by the cisternal and ventricular route is now frequently advised, and often with therapeutic success. Many points of contention are still open for discussion. By far the most important relates to the source of cerebrospinal infection following or accompanying septicemia. The older conception held by many was that organisms gained entrance to the subarachnoid space directly from the veins, capillaries or lymphatics. The argument of Lewkowicz,[3] however, that hematogenous meningitis begins primarily as ventriculitis is worthy of careful study. This worker boldly tapped the ventricles early in meningitic infections, instead of postponing this procedure until forced to do so by the development of subarachnoid blocking. With few exceptions, he finds the ventricles invaded by organisms early as well as late in the disease. From these findings and many others, he argues that the bacteria gain entrance to the meninges through the choroid plexus; and the meningitis is really only a sequela of ventriculitis. Howell and Cohen [4] both hold the same view and state: "Now we consider it proper to give early intraventricular serum, especially if the fluid withdrawn is turbid, indicating a ventriculitis, which commonly occurs in the first few days of the meningeal stage, if indeed the ventricles may not be the first location attacked." This contention is of such great significance from the standpoint of serum therapy that it becomes our duty to repeat these observations by careful multilocular examination of the cerebrospinal fluid, especially during the early days of infection.

One thing is impressed on physicians attempting to follow with care the course of a meningitic infection; namely, that no proper conception of the course of the disease is to be had by repeated examinations of the

3. Lewkowicz, K.: Le traitement specifique de la meningite epidemique, Arch. de méd. d. enf. **27**:193 (April) 1924.

4. Howell, W. W., and Cohen, A. A.: Intraventricular and Subdural Serum Treatment of Meningococcus Meningitis in Infancy, Am. J. Dis. Child. **24**:427 (Nov.) 1922.

lumbar fluid alone, and that with the further progress of the disease lumbar fluid analyses become progressively less satisfactory, for the reason that the products of inflammation, as found in the lumbar sac, do not adequately represent the course of the infection throughout the cerebrospinal fluid system.

Tubercular Meningitis.—It has been found by a number of observers and by us that the fluid obtained at cistern puncture may contain more organisms and more cells than that from lumbar puncture.

Spinal Subarachnoid Block.—Perhaps the most satisfactory use of combined puncture methods is in the detection of spinal subarachnoid block.

The loci to be tapped should depend on the supposed location of the lesion. If a compression of the spinal cord is suspected, cisternal-lumbar puncture is indicated; if the lesion seems to be distal to the conus, that is, below the first lumbar vertebra, then double lumbar puncture should be performed. In doubtful cases the operator should be prepared to examine the fluid at as many levels of the lumbar sac as is indicated, in conjunction with cistern puncture or not. French writers state that the spinal subarachnoid space may be entered at all levels, and they apparently use cervical and thoracic punctures with impunity. We have not done this, except that on a number of occasions we have punctured without hesitation between the twelfth thoracic and first lumbar vertebrae.

Whatever the loci selected for puncture, the object to be attained is to tap the subarachnoid space above and below the lesion.

It was shown as early as 1913, by Marie, Foix and Robert [5] that there is marked difference in the spinal fluid above and below a compression of the spinal cord. Further studies have confirmed this fact. It is now apparent that the fluid below a tumor or level of compression from other cause presents an increase in protein, at times of extremely high degree; and further, that the amount of protein varies little throughout the cavity below the block.

Above the level of compression the condition is somewhat different. Immediately above the block the protein is abnormal, although much less in amount than that below; this increase in protein lessens progressively, the higher in the spinal canal the fluid is examined; yet even in the cisterna magna an increase in protein may frequently be found.

Many of the fluids below a compression of the spinal cord show xanthochromia; a few show the complete Froin syndrome. A great many more are clear and colorless, the only recognizable pathologic find-

5. Marie, Foix and Robert: Service que peut rendre la punction rachidienne pratiquee a des etages differents pour la diagnostic de la hauteur d'une compression medullaire, Rev. neurol., 1913, 712.

ings being an hyperalbuminous state. To bring out the significance of increased protein, that is, stasis below a tumor or other compression, a comparison with the fluid above is recommended, together with dynamic studies to demonstrate physiologically a blocking of the spinal fluid pathway. This is readily accomplished by combined cisternal-lumbar puncture, a method that has found advocates not only here but abroad.[6]

Tumors of the Cauda Equina.—It is not always possible to obtain fluid from below tumors situated low in the lumbosacral canal. In such tumors the fluid directly above has been found to be yellow and charged with a large amount of protein. A second puncture above the first will show the protein content less in amount, but even in the cisterna magna, an abnormal fluid may be obtained. While such fluids are similar to those found below cord tumors, usually two observations will serve to differentiate them—the amount obtained from above a cauda tumor is large in amount, 10 or 15 c.c., whereas it is often impossible to obtain as much as 5 c.c. below a tumor; most important, there is no evidence of block of the spinal fluid pathways as demonstrated by the manometers, both being above the tumor.[7]

That increased protein, even when accompanied by xanthochromia, with absence of signs of block, is not a reliable guide to the existence of cauda tumor is admitted, but that these findings frequently accompany cauda tumors is equally certain (Chart 5).

Our present use of the spinal fluid abnormalities in the detection and localization of spinal subarachnoid block may be summarized as follows: (1) When cord-compression is suspected, lumbar puncture is performed and dynamic studies carried out, special emphasis being placed on Ayala's index (ratio of quantity of fluid withdrawn to drop in pressure) and Queckenstedt's sign (compression of the jugular veins). Also a rough protein test is carried out at the bedside. If the fluid is yellow, obtained only in small quantity, shows no pressure-rise on jugular compression, and contains an enormous amount of protein, then we feel safe in considering it a "compression fluid." (2) When the fluid is clear and colorless, normal in amount, shows a pressure-rise—although perhaps delayed—on jugular compression, and contains only a moderate excess of protein, then we immediately puncture the cisterna magna, the field of operation having been previously prepared, in order to obtain fluid

6. Ayer, J. B.: Puncture of the Cisterna Magna, Arch. Neurol. & Psychiat. **4**:529 (Nov.) 1920. Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Puncture, ibid. **7**:38 (Jan.) 1922. Eskuchen, K.: Die Diagnose des Spinalen Subarachnoidalblocks, Klin. Wchnschr. **3**:1851 (Oct. 7) 1924.

7. Cushing, H., and Ayer, J. B.: Xanthochromia and Increased Protein in the Spinal Fluid Above Tumors of the Cauda Equina, Arch. Neurol. & Psychiat. **10**:167 (Aug.) 1923.

for comparison and in order to carry out our dynamic studies more accurately. (3) If we find a block, partial or complete, in a case in which the level is doubtful, the head is slightly raised, and 1 c.c. of lipiodol is injected into the cisterna magna for roentgen-ray evidence of the level of block. It is found that in approximately one half of the cases cisterna puncture is not necessary, and that in only one quarter of the cases lipiodol is required.

"FRACTIONAL" EXAMINATION OF THE SPINAL FLUID

Fractional examination is the name given by a number of German writers [8] to examinations of the fluid when the first and last portions withdrawn are compared. As all who have examined fluids know, there is a slight difference in the first and last portions, even when as little as 10 c.c. is withdrawn. It is found that when puncture has been performed while the patient is seated and a large amount of fluid has been taken, 30 c.c. or more, striking differences are seen in the first and last tubes. It has been estimated that the spinal canal holds on an average 77 c.c. It is reasonable, then, that after withdrawal of half of this amount the findings in the last fluid taken should differ from that of the first, showing a greater pathologic process when the lesion is mainly cerebral and less when it is chiefly spinal.

In our experience fractional examinations have shown only quantitative differences—which is all that is claimed for the method—and that the first and last portions are never radically different. We, therefore, feel that the differences shown by combined punctures are much more reliable than fractional examination of the lumbar fluid. However, the fact that the pathologic condition of the fluid changes quantitatively during withdrawal at any locus of the cerebrospinal space, is a principle not to be forgotten.

EVIDENCE OF INTERCHANGE OF FLUID AT DIFFERENT LOCI

The various experiments of intravital staining by the introduction of dyes into the cerebrospinal fluid spaces, as performed by Weed [9] and others, have shown that substances thus injected are not uniformly distributed throughout the fluid spaces, and tend to gather in one area or another. Experiments by Solomon, Thompson, and Pfeiffer [10] showed

8. Weigeldt: Footnote 2. Eskuchen, K.: München. med. Wchnschr. **69**: 1536, 1922. Weinberg, F.: München. med. Wchnschr. **68**:577, 1921.

9. Weed, L. H.: Studies on Cerebrospinal Fluid, J. M. Res. **31**:21 (Sept.) 1914 (New Series Vol. 26).

10. Solomon, H. C.; Thompson, L. J., and Pfeiffer, H. M.: Circulation of Phenolsulphonephthalein in the Cerebrospinal System, J. A. M. A. **79**:1014 (Sept. 23) 1922.

that when phenolsulphonephthalein was introduced into the lumbar subarachnoid space, with the patient in a horizontal position, it tended to diffuse slowly toward the cisternal region, and very little made its way into the cerebral ventricles. On the contrary, the dye injected into the lateral ventricles tended to make its way into the cisternal and lumbar regions.

Young and Alpers [11] showed a similar discrepancy between the fluid in the two spaces by a different method. They injected Swift-Ellis serum into the lumbar subarachnoid space, the cisternal subarachnoid space and the lateral ventricle. The introduction of this serum leads to the production of an aseptic meningitis. When the fluid was injected into the lumbar subarachnoid space or into the cisternal subarachnoid space, it was followed by a rise in protein content and cells in both the lumbar and cisternal regions, but there was little or no evidence that this reaction reached the ventricles. When the serum was injected into the ventricles, it was found that there shortly appeared an increase of these substances in the cisternal and lumbar spaces.

CONCLUSIONS

The cerebrospinal fluid from various loci may differ in constitution even in the absence of evidence of block. This is well shown in cases of general paralysis. In cases in which there is interference with movement of the fluid, the constituents of the fluid from several loci may be very diverse.

Examination of the cerebrospinal fluid from loci other than the lumbar sac is proving of increasing value in our understanding of a number of pathologic states. The methods of combined punctures especially offer a diagnostic opportunity impossible from a study of lumbar fluid alone.

In the use of therapeutic agents to be introduced into the cerebrospinal fluid, it is often of great importance to take advantage of several possible points of entrance, especially when there may be adhesions.

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11. Young, A. W., and Alpers, B. J.: The Protein and Cellular Content of the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **12**:537 (Nov.) 1924.

REDUCTION OF NORMAL CEREBROSPINAL FLUID PRESSURE BY INTRAVENOUS ADMINISTRATION OF HYPERTONIC SOLUTIONS

EXPERIMENTAL STUDIES ON CATS *

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In 1919, Weed and McKibben [1] called attention to the fact that it was possible to decrease the pressure of the cerebrospinal fluid experimentally by the intravenous injection of hypertonic solutions. Since the publication of their paper a number of workers have confirmed their findings and contributed some further observations.

Haden [2] was the first to publish his clinical application of this principle. He administered a concentrated glucose solution to two patients with meningitis and obtained some improvement in their condition, which he attributed to a lowering of the intracranial tension. Cushing and Foley [3] followed this with a demonstration of the possibility of decreasing the brain volume by the intravenous injection of hypertonic solutions. These authors further found that a similar diminution in brain bulk and decrease in intracranial pressure could be obtained by the introduction of hypertonic solutions into the stomach or intestine. Hypotonic solutions, which had been shown by Weed and McKibben to increase the brain mass as well as the cerebrospinal fluid pressure when administered intravenously, were found by Cushing and Foley to have a similar though less pronounced action when introduced into the intestine.

Sachs and Belcher [4] were able to ameliorate the increased intracranial tension occasioned by a brain tumor through the intravenous injection of a concentrated (100 c.c. of a 35 per cent.) sodium chlorid solution.

In 1920, Foley and Putnam [5] confirmed the original work of Weed and McKibben, and also demonstrated that the introduction of hyper-

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* Read at the meeting of the Association for Research in Nervous and Mental Diseases, December, 1924.

1. Weed and McKibben: Am. J. Physiol. **48**:512, 1919.

2. Haden: Therapeutic Application of the Alteration of Brain Volume, J. A. M. A. **73**:983 (Sept. 23) 1919.

3. Cushing and Foley: Proc. Soc. Exper. Biol. & Med. **17**:217, 1920.

4. Sachs, Ernest, and Belcher, George W.: Use of Saturated Salt Solution Intravenously During Intracranial Operations. Preliminary Report, J. A. M. A. **75**:667 (Sept. 4) 1920.

5. Foley and Putnam: Am. J. Physiol. **53**:464 (Oct.) 1920.

tonic solutions into the gastro-intestinal tract would produce similar results. They advised administration by this route not alone because of its convenience, but also because of its safety. Disturbances of circulation and respiration which were frequently encountered on intravenous injection were avoided in this way. Thirty per cent. sodium chlorid solutions were found to be most effective. A saturated solution of sodium sulphate produced similar results, though less extensive and of slower rate. Concentrated dextrose was less satisfactory, producing still slower and less marked reductions. These authors further believe that the decreased intracranial tension is not due solely to the decrease in brain volume, but primarily represents "new ratios between secretion and absorption of cerebrospinal fluid."

Ebaugh and Stevenson [6] made observations on an epileptic patient who had a defect in his skull occasioned by a subtemporal decompression operation. They confirmed the former observations that hypertonic solutions administered intravenously or orally produced a fall in intracranial pressure. They likewise found a distinct rise in pressure after the ingestion of from 4 to 8 liters of water. Two hundred cubic centimeters of a 30 per cent. dextrose solution given intravenously was followed by a fall in pressure which was more gradual and less marked but more prolonged than that following a sodium chlorid solution.

Sachs and Malone [7] recorded a decrease in the brain volume in dogs following the intravenous administration of a 30 per cent. sodium chlorid solution. Within ten minutes a change was noted, which reached its maximum in from forty-five to sixty minutes. They found that the rate of administration should not exceed 1 c.c. a minute, since when it was given more rapidly there was likely to be a fall in blood pressure and respiratory disturbance. These workers also used a 30 per cent. glucose solution, but without effect.

In 1921, Weed and Hughson [8] published the results of more extended experiments, and they conclude that while normal cerebrospinal fluid pressure is partially dependent on cerebral venous pressure and to a less extent on cerebral arterial pressure, it is for the most part independent of either. They also state that the alterations in cerebrospinal fluid pressure following intravenous administration of hypertonic solutions, while partially parallel to the variations in cerebral arterial and venous pressures, are mainly independent of them and show much more marked depressions.

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6. Ebaugh and Stevenson: Bull. Johns Hopkins Hosp. **31**:440, 1920.
7. Sachs and Malone: J. Physiol. **55**:277, 1921.
8. Weed and Hughson: Am. J. Physiol. **58**:53, 85 and 101, 1921-1922.

Dowman,[9] in a clinical application of this principle, advises the use of hypertonic solutions in selected cases of brain injury. He has found it especially valuable in conditions in which there has been brain damage with gradually increasing intracranial pressure. He advises the repeated administration of one-half ounce of a saturated solution of magnesium sulphate by mouth or from 30 to 50 c.c. of a 30 per cent. sodium chlorid solution by vein. In a patient with evidence of marked increased intracranial pressure, the symptoms were relieved in thirty-six hours by repeated injections of salt solution.

Fay[10] found that the intestinal installation of magnesium sulphate was almost twice as efficient as sodium chlorid for the reduction of intracranial pressure. This he attributes to the fact that magnesium sulphate is nondialyzable while sodium chlorid is readily dialyzed. He also points out that the administration of sodium chlorid may produce a secondary wave of edema and increased intracranial pressure owing to its absorption and mobilization in the tissues with a subsequent attraction of fluid from the blood stream. Fay calls attention to the fact that overdehydration is possible and may be serious, if not fatal.

OBJECT OF STUDY

When I began this work, I felt that the following points had been satisfactorily established:

1. The intravenous administration of some hypertonic solutions will cause a definite fall in cerebrospinal fluid pressure and diminution of brain volume.

2. The fall in cerebrospinal fluid pressure is usually accompanied by a moderate decrease in the systemic venous pressure. The intracranial pressure may be influenced by this venous pressure depression, but is mainly independent of it.

3. The installation of certain hypertonic solutions into the gastrointestinal tract will produce results similar to those obtained by intravenous administration.

The object of my studies was to determine if possible which solutions were least toxic and most efficient in lowering intracranial pressure when given intravenously.

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9. Dowman, C. E.: Management of Head Injuries, J. A. M. A. **79**:2212 (Dec. 30) 1922.

10. Fay, T.: Administration of Hypertonic Salt Solutions for Relief of Intracranial Pressure, J. A. M. A. **80**:1445 (May 19) 1923; Comparative Values of Magnesium Sulphate and Sodium Chlorid for Relief of Intracranial Tension, ibid. **82**:766 (March 8) 1924.

EXPERIMENTAL METHODS

I used cats in my experiments. They were anesthetized with ether by the intratracheal method. This anesthetic has been found suitable by other workers who demonstrated that with it constant pressure readings were obtained over long periods when an even depth of anesthesia was maintained. My experiments have confirmed this.

The cerebrospinal fluid pressures were registered on a glass manometer connected to the lumbar puncture needle by a rubber tube and adaptor tip. The manometer was filled with Ringer's solution and adjusted so that the top of the column of Ringer's solution was at a point 125 mm. above the level of the point of entrance into the subarachnoid space. A lumbar puncture needle was introduced into the cerebellomedullary cistern by piercing the occipito-atlantoid ligament; it was connected with the filled manometer system as soon as the obturator in the needle was removed and before more than two or three drops of spinal fluid had escaped. In this way more accurate pressure determination can be made than when the spinal fluid must fill the empty manometer. Records of pressures were made at three minute intervals, and were recorded as millimeters of Ringer's solution. No records were made unless there was free pulsation in the manometer. When the anesthetic is administered with a cone, there is ordinarily an excursion of about 4 mm. with each respiration and about 1 mm. for the heart beat. With the intratracheal method of anesthesia, the respiratory variation is much less marked. An absence of this pulsation usually indicates some block in the manometer system.

The normal pressure values have been given as averaging 112 mm. by Becht,[11] 119 mm. by Weed and McKibben and 133 mm. by Foley and Putnam. The discrepancy may be due to the fact that Becht and Weed and McKibben apparently used empty manometers, while Foley and Putnam filled the manometer with physiologic sodium chlorid. The average pressure in my series of experiments was 127 mm.

The administration of hypertonic solutions was made in the femoral vein, either with a syringe or from a buret. The rate of inflow was regulated so that 1 c.c. was introduced per minute. This, after much experimentation, was determined as the satisfactory rate. More rapid injection of some solutions was likely to produce respiratory paralysis.

In order to standardize the dosage, 10 c.c. of a 25 per cent. solution was usually employed. When the salt would not form a solution of this percentage, a saturated solution was used. The observations were carried out over perods of one or two hours.

EXPERIMENTAL RESULTS

Sodium Bicarbonate.—Sodium bicarbonate would not be expected to produce marked pressure alterations, as a saturated solution is of such low concentration. The concentration being only 9 per cent., 20 c.c. were used in the experiments.

During the period of injection there is a sharp rise in cerebrospinal fluid pressure of from 40 to 50 mm., which is followed by a sharp drop. The initial pressure is restored about five minutes after the injection starts, and the fall continues for from thirty to forty minutes, when the

11. Becht: Am. J. Physiol. **50**:1 (Feb.) 1920.

lowest point is reached. In the experiment shown (Fig. 1), the fall was from an original pressure of 125 to a minimum of 78 mm., a fall of 47 mm. At the end of 45 minutes, there was a gradual rise, which was not followed to its completion. No disturbances of respiration or heart action were observed during or after the administration. This solution is not toxic for cats, but it is not suited for lowering cerebrospinal pressure because of its low solubility.

Sodium Sulphate.—This salt was used in a 25 per cent. solution. Ten cubic centimeters intravenously produces a prompt rise of cerebrospinal fluid pressure of 40 to 50 mm. during the period of injection, which is only slightly greater when 20 c.c. is injected. This is followed by a rather prompt fall, the pressure reaching the original level in about six minutes and its lowest point in from thirty to forty minutes (Fig. 2).

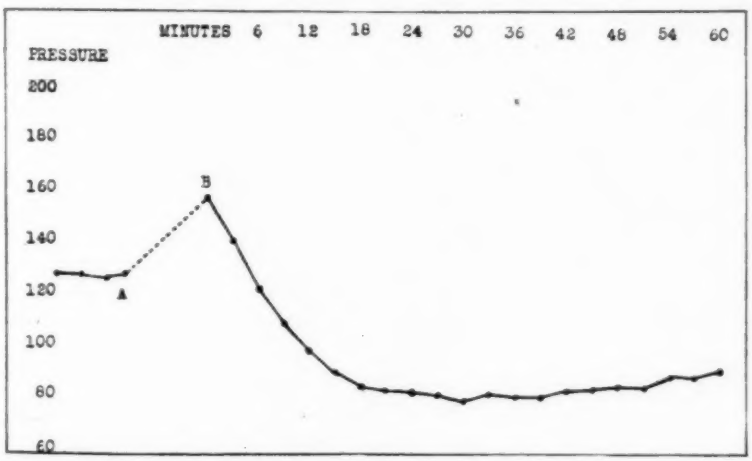

Chart 1.—Cat, weighing 2,900 gm. *A* and *B*, 20 c.c. of 9 per cent. sodium bicarbonate was given intravenously.

The lowest level is usually above zero.[12] No disturbances of respiration, or cardiac action and no convulsive twitchings were ever noted. In one experiment, 50 c.c. of a 25 per cent. solution were given intravenously in less than five minutes, without the slightest disturbance. The pressure rose from 125 to 198 mm. when the pulsations ceased in the manometer, and it was evident that the system was blocked. The animal was kept under anesthesia for one hour and forty minutes, and was still in good condition at the expiration of that time.

Weed and McKibben noted the absence of any disturbance during the administration of sodium sulphate, but had several animals die later

12. Negative pressures of from 5 or 10 mm. have been noted at times by all observers.

during their observations apparently from the toxic effects of this salt. I have not observed this, though I have not finished the work I expect to do with this substance.

Sodium Chlorid.—Sodium chlorid solutions produce the most striking curves of any solution I have used. Ten cubic centimeters of a 25 per cent. solution was used in most of the experiments. There is a marked rise in pressure during the injection, which may reach 75 to 80 mm. and is usually over 40. This is followed by a prompt and sharp fall, the pressure usually reaching the original level within five minutes and going to zero in from twenty to twenty-five minutes (Fig. 3). With this salt negative pressures are at times produced, and the lowest point is generally reached within thirty minutes. Unless the injection is made

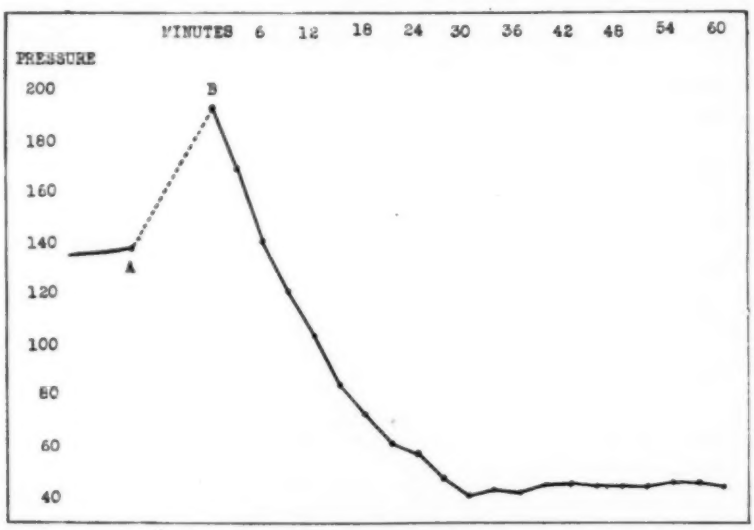

Chart 2.—Cat, weighing 2,660 gm. *A* and *B* (10 minutes), 10 c.c. of 25 per cent. sodium sulphate was given intravenously.

slowly, serious respiratory disturbances are observed, as well as cardiac irregularity and convulsions. These may be noted when no more than 1 to 2 c.c. have been injected. Sudden cessation of respiration and death are likely to occur. These toxic effects have been noted by practically all observers who have done experimental work in this field. It is the consensus of opinion that this danger is mainly obviated by very slow administration. No death has occurred in my experience in which the administration was not faster than 1 c.c. a minute and when not more than 10 c.c. of a 25 per cent. solution was given. The rate of 1 c.c. a minute, however, is very slow, and is likely to be exceeded unless one is extremely careful.

Weed and Hughson used a concentrated solution of salts in the proportions used in Ringer's solution, in which the sodium chlorid, potassium chlorid and calcium chlorid were twenty times the concentration of the normal solution. This gives a sodium chlorid concentration of 18 per cent. With this solution these authors found no toxic effects. The lowering of the pressure, however, was not so great as with a 30 per cent. sodium chlorid solution, a fact which was borne out by my experiments.

In order to determine satisfactory reduction free from the dangers of the pure sodium chlorid solution, some experiments were undertaken

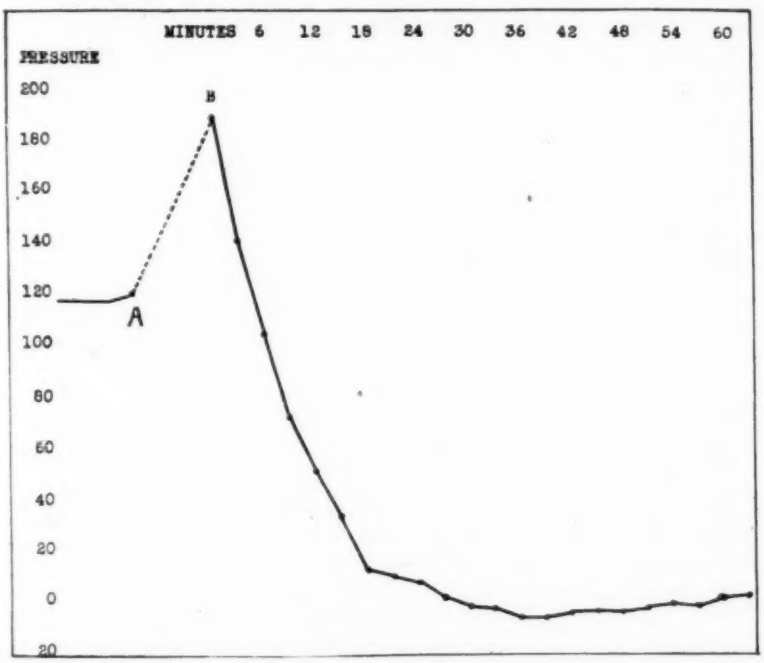

Chart 3.—Cat, weighing 2, 000 gm. *A* and *B* (10 minutes), 10 c.c. of 25 per cent. sodium chlorid was given intravenously.

with a more concentrated solution of the salts used in the Ringer-Locke solution (Fig. 4). The ingredients were multiplied by 22.7, which gives the following formula: sodium chlorid, 25 per cent.; potassium chlorid, 1.16 per cent.; calcium chlorid, 0.69 per cent. The results with this solution were mainly disappointing. It did not seem to be much less toxic than the pure sodium chlorid solution of the same concentration, and the reduction of cerebrospinal fluid pressure was not so great. Even 2 or 3 c.c. of this solution, if not injected very slowly, produced interference with respiration. In one 2,840 gm. cat, 42 c.c. of this solution caused death. In this experiment 10.5 gm. of sodium chlorid were

administered, which is 3.7 gm. per kilogram of body weight. This is the estimated lethal dosage of pure sodium chlorid administered in a 10 per cent. solution as given by Münzer.[13] This percentage cannot be taken as a standard, however, as it is subject to marked variations.

That sodium chlorid is very toxic to protoplasm has long been known, and it was first demonstrated by Ringer that a frog's heart perfused with an isotonic solution of sodium chlorid would gradually lose its excitability and cease to beat. He found that when a certain proportion of calcium chlorid was added, the excitability returned and spontaneous contractions again occurred. Relaxation, however, was imperfect; and it was found that this could be obviated by adding a small amount of potassium chlorid. It was hoped that a well buffered solution of this kind would be more suitable for this purpose than a pure sodium chlorid solution. In order to determine this, a concentrated solution of the salts

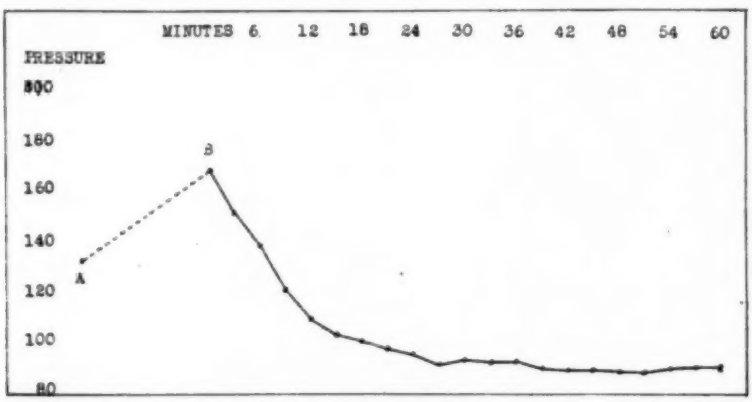

Chart 4.—Cat, weighing 2,100 gm. *A* and *B*, 15 c.c. of 18 per cent. Ringer's solution was given intravenously (NaCl, 18 per cent.; KCl, .84 per cent.; $CaCl_2$, .48 per cent.).

used in Tyrode's solution was made according to the following formula: sodium chlorid, 25 per cent.; potassium chlorid, 0.625 per cent.; calcium chlorid, 0.625 per cent.; magnesium chlorid, 0.3,125 per cent.; acid sodium phosphate, 0.156 per cent.; sodium bicarbonate, 3.125 per cent.; dextrose, 3.125 per cent. Ten cubic centimeters of this solution, injected intravenously, produced a satisfactory lowering of pressure. No immediate disturbances were noted when it was injected rapidly, which was an improvement over the pure sodium chlorid or concentrated Ringer's solution. In six experiments, however, all of the animals died before the expiration of two hours.

Sodium Bromid.—A 25 per cent. solution of sodium bromid injected intravenously was found to be toxic, from 2 to 4 c.c. usually producing

13. Münzer: Arch. f. Exper. Path. **41**:74, 1898.

paralysis of respiration. In one experiment the toxic dose was calculated as 0.22 gm. per kilogram.

Magnesium Sulphate.—As would be expected, magnesium sulphate, injected intravenously, is extremely toxic. From 2 to 5 c.c. of a 25 per cent. solution is lethal to an average sized cat. In one instance

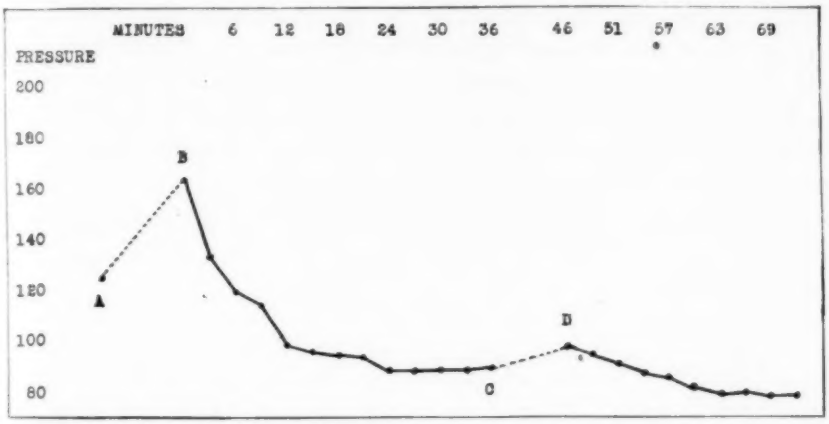

Chart 5.—Cat, weighing 3,200 gm. *A* and *B*, 10 c.c. of 25 per cent. sodium citrate was given intravenously; *C* and *D*, 10 c.c. of 25 per cent. sodium citrate was given intravenously.

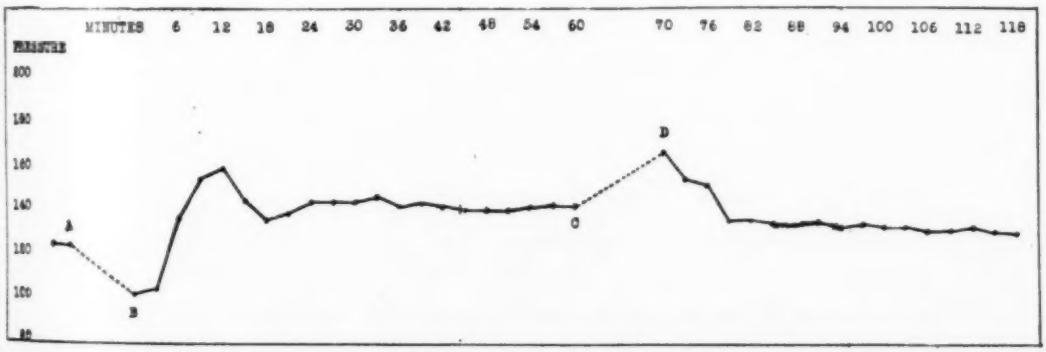

Chart 6.—Cat, weighing 2,800 gm. *A* and *B* (10 minutes), 10 c.c. of 25 per cent. solution sodium tartrate was given intravenously; *C* and *D* (10 minutes), 10 c.c. of 25 per cent. solution of sodium tartrate was given intravenously.

death was produced by 0.18 gm. per kilogram of body weight. Death may be preceded by a short convulsion, or be caused by sudden cessation of respiration.

Calcium Lactate.—A saturated solution of calcium lactate produced a sharp rise in cerebrospinal fluid pressure during the injection. In one instance it rose from 154 to 240 mm. as 5 c.c. of this solution was

injected, at which time the sudden death of the cat terminated the experiment. The same solution was tried with two other cats, but in each instance death occurred before more than 5 c.c. had been administered.

Calcium Chlorid.—A 25 per cent. solution of this salt was unsatisfactory. In three small cats weighing from 1,800 to 2,000 gm., death occurred during administration before 5 c.c. had been given. In these animals there was no appreciable change in pressure. In one 3,060 gm. cat there was a slight convulsion when 3.5 c.c. had been given, and paralysis of respiration occurred at 9.5 c.c., which is 0.77 gm. of calcium chlorid per kilogram of body weight. In this instance the spinal fluid pressure rose from 114 to 132 mm.

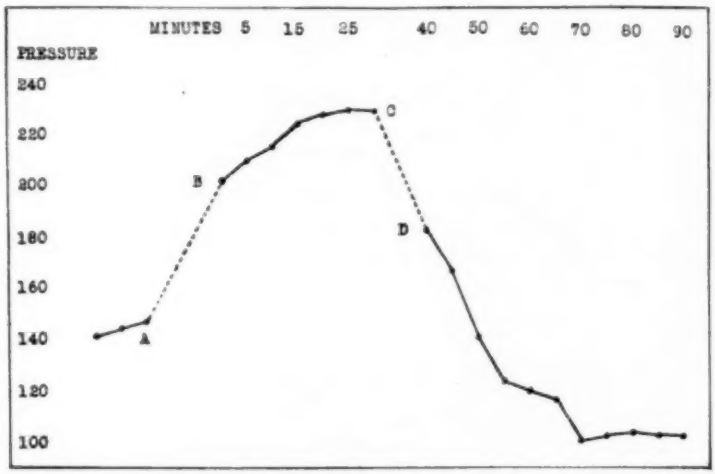

Chart 7.—Cat, weighing 2,260 gm. *A* and *B* (15 minutes), was given 50 c.c. of distilled water intravenously; *C* and *D* (10 minutes), was given 10 c.c. of 100 per cent. dextrose solution intravenously.

Sodium Citrate.—The intravenous administration of a 25 per cent. solution of sodium citrate is accompanied by a rise in cerebrospinal fluid pressure. In the experiment shown in the diagram (Fig. 5), this amounted to 40 mm. Within six minutes the pressure had regained the original level. It gradually descended to 88 at twenty-four minutes, and continued at this level for twelve minutes, when a second injection of 10 c.c. was made. This produced very little change. Sodium citrate does not seem to be toxic in average dosage, though no experiments have been made with rapid injection. It is not very effectual in depressing intracranial pressure.

Sodium Tartrate.—Sodium tartrate is the least effectual substance I have used so far. During the administration, in the instance charted (Fig. 6), there was a slight fall in pressure, after which there was a

rise of 45 mm. in twelve minutes. Subsequently, there was a fall of 20 mm. with a continuation of about this pressure, which was from 18 to 20 mm. above the original reading, for an hour. It is not toxic and even when administered rapidly, it produces no disturbance.

Dextrose.—A good many experiments have been made with dextrose. With 10 c.c. of 25 or 30 per cent. solutions, no appreciable results have been obtained. With 10 c.c. of a 100 per cent. solution, marked depressions in pressure have been observed (Figs. 7 and 8).

During the injection, there is frequently a rise in pressure which may average from 40 to 50 mm., but which is frequently much less. The rise terminates with the end of the injection, and the fall commences

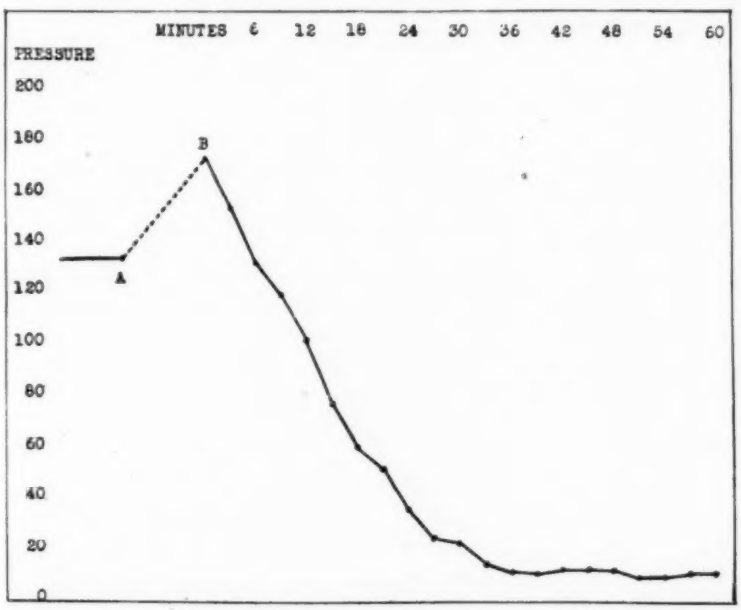

Chart 8.—Cat, weighing 1,850 gm., was given 10 c.c. of 100 per cent. dextrose intravenously (*A* and *B*, 10 minutes).

within three minutes. The fall is a little more gradual than with some of the salts, especially sodium chlorid, and it requires from thirty to forty minutes for the pressure to reach its lowest point. If this is above zero, it may be depressed further by additional doses. The depression is maintained for more than two hours, which is as long a period as I have observed.

Dextrose is absolutely nontoxic, and I have never seen it result in the slightest disturbance of respiration or cardiac action, no matter how much was given or how quickly it was administered. I have given 50 c.c. of a 100 per cent. solution in less than one minute without any untoward action.

CONCLUSIONS

Experiments have been made to determine the effect of the intravenous administration of various hypertonic solutions on the cerebrospinal fluid pressure of cats. Concentrated solutions of sodium bicarbonate, sodium sulphate, sodium citrate, sodium chlorid, sodium bromid, calcium lactate, calcium chlorid, magnesium sulphate and dextrose have been used. A few observations with a combination of electrolytes have also been made in the proportions given in the Ringer-Locke and Tyrode solutions. Sodium bromid, calcium lactate, calcium chlorid and magnesium sulphate were found to be too toxic. Sodium citrate, sodium tartrate and sodium bicarbonate were relatively ineffective. Sodium sulphate, sodium chlorid, concentrated Ringer-Locke solution and concentrated Tyrode solutions and dextrose produced satisfactory depressions. Sodium sulphate was nontoxic at first but has been reported by Weed and McKibben to have caused death later, and so is unsafe for clinical use. Sodium chlorid produced the most pronounced decrease in intracranial pressure of any substance used, but it is toxic unless administered very slowly. Furthermore, as it is later mobilized in the tissues producing a secondary wave of edema, as shown by Fay, it is considered unfit for general clinical administration. The same objections apply to concentrated Ringer-Locke and Tyrode solutions although they are somewhat less toxic.

Dextrose is the only substance of this group which is nontoxic and produces a satisfactory fall in intracranial pressure.

THE CEREBROSPINAL FLUID IN LEAD POISONING *

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Notwithstanding restrictive and protective regulations and more or less effective educational endeavors, lead poisoning continues to hold its place in the first rank of industrial hazards, and to find its victims through the most unexpected avenues among the nonindustrial population as well. It is a question whether there has been any material decrease in the incidence. Much has been accomplished in protecting workers in such hazardous trades as white lead manufacture, painting with hand brushes, pottery glazing, type founding and file cutting. At the same time, however, there has been a phenomenal growth of new industries using lead, such as the storage battery industry, and the adoption of new mechanical processes, such as spray painting and machine type setting, which introduce new types of industrial hazards. Entirely new uses for certain organic compounds of lead have arisen which may give them nearly universal application, and these, too, must be taken into account. Moreover, conditions of previously unknown etiology are from time to time added to the list of lead diseases. A notable example appears to be the serous meningitis, so-called, of young children in the Far East. This, said by Suzuki and Kaneko [1] to be the fourth in rank among the important causes of infant mortality in Manchuria, was found by Hirai,[2] in 1923, to be due to the lead-containing powder used as a cosmetic by young mothers.

Although involvement of the nervous system in lead poisoning was known to early medical writers, real appreciation of its importance is a matter of relatively recent date. Ramazzini,[3] in 1700, had written of potters that "first their hands begin to shake and tremble and then they become paralytic, splenetic and lethargic," but Tanquerel des Planches,[4]

* From the Department of Pathology, University of Michigan.

1. Suzuki, T., and Kaneko, J.: Serous Meningitis in Infants from Lead Poisoning, J. Oriental Med. **11**:55-67, 1924.

2. Hirai: Zikahassi, 1923, quoted by Suzuki and Kaneko.

3. Ramazzini, Bern: De morbis artificium diatriba, Editio quarta, Opera omnia **5**:16, 1739.

4. Tanquerel des Planches, L.: Lead Diseases, 1839. (Dana, S. L., 1850.)

in 1839, by the collection, analysis and discussion of seventy-two cases of lead encephalopathy, firmly established the nosology of this condition. From that date the literature has multiplied with great rapidity until there are now about 300 titles dealing specifically with lead encephalopathy. Concealed under less definite titles are numerous other clinical reports. Among these cases, with their great variation in symptomology, are many in which evidences of meningeal involvement appear, sometimes dominating the clinical picture. Thus the terms saturnine meningitis and saturnine meningo-encephalitis came to be applied to certain cases in which lead was thought to play at least a contributory part. Such were those reported by Lyman [5] and by Bensaude and Rivet,[6] the former in 1891 and the latter in 1904.

Mosny and Malloizel [7] were the first to establish a morphologic basis for a clinical saturnine meningitis. Writing in 1904, they described the practically constant occurrence in cases of lead poisoning of a lymphocytosis of the cerebrospinal fluid. In various patients these authors found 5 to 15, 3 to 6, 4 to 11, 1 to 2 and 9 to 23 lymphocytes per field. During an encephalopathic crisis the last of these patients showed as many as 111 lymphocytes per field. They conclude: "It is possible, through examination of the cerebrospinal fluid, to measure, as it were, the impregnation of the nervous system by lead, to assign to their true cause similar nervous manifestations, and, finally, to give to the worker such advice as will enable him to safeguard his health." The occurrence of a type of lead encephalopathy characterized, among other things, by the presence of a lymphocytosis of the cerebrospinal fluid, was henceforth recognized by the French clinicians [8] who, during the next eight

5. Lyman, H. M.: Chronic Meningo-encephalitis Complicated with Lead-Poisoning, Internat. Clin. **11**:252-262, 1891.

6. Bensaude, R., and Rivet, L.: Un cas de méningite aiguë syphilitique, Arch. gen. de med. **194**:2766, 1904.

7. Mosny and Malloizel: Saturnisme et lymphocytose céphalorachidienne, Soc. de biol. **57**:211, 1904.

8. Mosny and Malloizel: Le méningite saturnine, Rev. de méd. **27**:505-531, 659-700, 1907. Mosny, E., and Harvier, P.: Héningo-encephalite aiguë, saturnine, suivie d'amaurose hysterique, Bull. et mém. Soc. méd. d. hôp. de Paris **24**:1344-1354, 1907. Mosny, E., and Pinard, M.: Méningite saturnine aiguë, Bull. et mém. Soc. méd. d. hôp. de Paris **25**:484-490, 1908. Bernard, L., and Troisier, J.: Cas d'intoxication saturnine avec méningite, anémie et ictere, Bull. et mém. Soc. méd. d. hôp. de Paris **25**:753-762, 1908. Pinard, M.: Étude clinique de la méningite saturnine, Gaz. d. hôp. **81**:963-968, 1908. Vigourau, A.: Méningo-encéphalite saturnine survenue chez un héréditaire dégenére, Bull. et mém. Soc. anat. de Paris **11**:217-220, 1909. Marie, A., and Beaussart, P.: Méninges syphilis et saturnisme, La Clinique, Paris **5**:117-122, 139-140, 1910. Loeper and Pinard, M.: Méningite saturnine aiguë précoce (forme méningitique complète), Bull. et mém.

Footnote 8 continued on following page.

years, published numerous articles dealing with the signs and symptoms of saturnine meningo-encephalopathy.

During this period of great interest in saturnine meningitis on the part of the French clinicians, Spiller,[9] in this country, had emphasized the meningeal endothelial proliferation in a painter who had shown evidence of central nervous system changes during life. No report of the state of the cerebrospinal fluid was made. Maas [10] likewise reported a group of cases which he believed exhibited a special form of lead encephalopathy, a hydrocephalus acquisitus which he called meningitis serosa in his title; but there was no report on the cerebrospinal fluid.

In the succeeding years there have been only occasional articles dealing with a meningeal reaction or with changes in the cerebrospinal fluid in cases of lead poisoning, but with the increasing elaboration of method of microchemical investigation, more complete studies of the fluid have been made.

Plate,[11] in 1913, reporting a case which he had diagnosed as meningitis saturnina, commented on the rarity of this condition as revealed by the German literature, and acknowledged his indebtedness to the French for the possibility of making the diagnosis. His patient showed a cerebrospinal fluid pressure of 440 mm. of water and a cell count of 258 on one occasion and 270 on another, almost all lymphocytes, falling to 14 in about seven weeks. In the same year, Boveri [12] discussed the meningeal reaction in chronic lead poisoning, and concluded that the meningeal reaction due to lead is manifested by an increase of pressure ranging from 30 to 50 cm. (Kroenig), by an increase in globulin content demonstrable by the Nonne and Noguchi tests and by a cellular reaction usually less pronounced than in tabes and general paresis.

Footnote 8 concluded from preceding page.

Soc. méd. d. hôp. de Paris **31**:226-229, 1911. Mosny, E., and Saint-Girons: Méningite saturnine subaiguë avec hémisparésie motrice passagère, Bull. et mém. Soc. méd. d. hôp. de Paris **31**:301-304, 1911. Widal, F.: Méningite saturnine, J. des practiciens **26**:228-230, 1912. De Massary and Vallery-Radot, P.: Paralysie saturine généralisée ayant debute par le type brachial avec lymphocytose rachidienne, Bull. et mém. Soc. méd. d. hôp. de Paris **33**:85-89, 1912. Leclerc, Palasse and Charvet: Méningite saturnine, Lyon méd. **118**:1044-1049, 1912. Braillon, Bax: Un cas mortel d'encéphalopathie saturnine; forme bulbaire de la méningite saturnine, Bull. et mém. Soc. méd. d. hôp. de Paris **33**:943, 1912.

9. Spiller, W. G.: The Pathological Changes in the Nervous System in a Case of Lead Poisoning, J. M. Res. **10**:142-152, 1903.

10. Maas, O.: Ueber eine besondere Form der Encephalopathia saturnina (Meningitis serosa), Monatschr. f. Psychiat. u. Neur. **30**:207-223, 1911.

11. Plate, E.: Ueber einen Fall von Meningitis saturnina, München. med. Wchnschr. **60**:2343-2344, 1913.

12. Boveri, P.: Le reazioni meningee nel saturnismo cronico, Riforma med. **29**:844, 1913.

In a case of fatal lead poisoning in a child of 5 years who had gnawed the paint from his crib, Thomas and Blackfan (1914 [13]) found on various occasions a clear, sterile cerebrospinal fluid with cells ranging from 20 to 40 per cubic millimeter, which were mostly mononuclears. The first puncture showed a greatly increased pressure, not subsequently noted. The Noguchi test was positive for globulin, Fehling's test was positive for reducing substance, and the Wassermann test was negative. A similar case in a 19 months old child was described by Strong [14] in 1920. The findings in three specimens of spinal fluid are reported in tabulated form. Slight increase in pressure was noted once. Cells were less than 10 in number on two occasions and less than 20 on the third. However, they were mostly polymorphonuclear. Tests for albumin, globulin and reducing substance were all positive in all three specimens.

In the second of the series of cases of lead meningo-encephalopathy reported in 1921 by Barron and Habein,[15] the cerebrospinal fluid was examined and found to be clear, with pressure slightly increased. There were 6 cells per cubic millimeter, and the Nonne, colloidal gold and Wassermann tests were all negative.

The following year, Norton [16] found in a baby poisoned by the lead acetate contained in an ointment applied to the mother's eczematous breast, a cerebrospinal fluid which was clear and faintly yellow, which gave positive globulin and sugar tests and showed a cell count of 12, of which 95 per cent. were polymorphonuclears. Three days later, when the child was still having convulsions, its fluid was clear, the pressure was much increased, the cell count was 30, of which 3 were polymorphonuclears and 27 lymphocytes, and there was also an increased globulin.

Kraffczyk (1923 [17]) reported three cerebrospinal fluid specimens from a lead worker known to have had chronic lead poisoning for fourteen or fifteen years, who gave evidence of a cerebellar ataxia and had frequent epileptiform convulsions. On the first occasion the fluid was clear, the pressure was 165 mm., albumin was increased, and there was a slight lymphocytosis. A little later the pressure was found to be

13. Thomas, H. M., and Blackfan, K. D.: Recurrent Meningitis, Due to Lead, in a Child of Five Years, Am. J. Dis. Child. **8**:377-380, 1914.

14. Strong, R. A.: Meningitis Caused by Lead Poisoning in a Child of 19 Months, Arch. Pediat. **37**:532-537, 1920.

15. Barron, M., and Habein, H. C.: Lead Poisoning, with Special Reference to Poisoning from Lead Cosmetics. Report of Four Fatal Cases of Encephalopathia Saturnina Occurring in One Family, Am. J. M. Sc. **162**:833-862, 1921.

16. Norton, N. R.: A Case of Chronic Lead Poisoning with Encephalitis, Internat. Clin., Series 32, **4**:231-233, 1922.

17. Kraffczyk, H.: Beitrag zur Symptomatologie der chronischen Bleivergiftung (cerebellare Ataxie nach chronischer Bleivergiftung), Deutsch. Ztschr. f. Nervenh. **80**:184-203, 1923.

250 mm., and the Nonne test, Phase I, was negative. Three years after the first puncture, the pressure was 100 mm., there was but a trace of albumin, and no cells were found.

Within the present year, the interesting paper of Suzuki and Kaneko,[1] to which reference has already been made, records the findings in the cerebrospinal fluid of two cases of so-called serous meningitis of infants, due in each instance to a white lead containing face powder, used by the mother. In the first infant there was a first pressure of 400 mm. of water, dropping to 200 mm. after the removal of 30 c.c. The fluid was clear. The Pandy and Noguchi tests and Nonne-Apelt, Phase I, were all positive, as was also the Haines test for sugar. The cell count was 4, equally divided between polymorphonuclears and small lymphocytes. The albumin content was found to be 0.066 per cent. and the calcium content 4.884 per cent. In the second case, the pressure was 400 mm., falling to 150 mm. Globulin tests were positive, albumin increased and the sugar test positive. The first cell count on this patient showed 6 lymphocytes, 14 polymorphonuclears; a later count showed 18 small lymphocytes, 30 polymorphonuclears and 4 red blood cells. One of these authors had previously reported on the increase of sugar in the cerebrospinal fluid in this type of meningitis.

This brief summary of the reported findings in the cerebrospinal fluid, while not complete, will suffice to show the trend of the observations that have been made. (A complete annotated bibliography is in course of preparation.) In Table 1 the reported data from some of the more important papers on this subject are arranged for comparison. It must be realized that such a study cannot deal rigidly with the facts recorded. One cannot, for example, with the data usually given, strike an average between cells "per field" or "per oil immersion field" and cells "per c.mm." One can, however, with some assurance, draw conclusions in regard to such facts as the presence or absence of a cellular increase and as to the type of cell concerned. The possibility of incorrect etiologic diagnoses must also be borne in mind. As far as can be ascertained, however, no cases have been admitted to this table in which evidence, such as known source of lead, red cell stippling or a lead line did not support the diagnosis. In view of the amount of information available, it is surprising that several of our monographic studies on the cerebrospinal fluid appearing within the past few years do not consider the changes in saturnine meningo-encephalopathy.

Inspection of the tabulated results shows that, in general, the three points emphasized by the French writers and accepted by Boveri,[12] Plate [11] and others still hold good. These are increased pressure, an increase in the number of cells, chiefly lymphocytes, and increased albumin (globulin) content. Each of these points requires a brief discussion.

TABLE 1.—*The Significant Changes in the Cerebrospinal Fluid in Reported Cases of Lead Meningo-Encephalopathy*

Author	Year	Pressure	Appearance	Cytology	Albumin	Globulin	Sugar
Mosny and Malloizel (Soc. de biol. **57**: 211, 1904)	1904	.....	.....	Lymphocytosis, 5-15, 3-6, 4-11, 7-11, 1-2, 9-23, per field; finally 111 in the last of the six cases	.....	.....	.....
Mosny and Harvier (Bull. et mém. Soc. méd. d. hôp. de Paris **24**: 1344, 1907)	1907	Increased	Clear and colorless	35-50 cells to oil immersion field; 95 per cent. polymorphonuclears	Slight	.....	.....
Bernard and Troisier (Ibid. **25**: 753, 1908)	1908	Flowing in rapid drops	Clear	About 20 lymphocytes and a few mononuclears per immersion field at a dilution of 1:16	0.60 gm. per liter	.....	.....
Mosny and Pinard (Ibid. **25**: 484, 1908)	1908	.....	.....	42 cells per oil immersion field, 96 per cent. lymphocytes	.....	.....	.....
Loeper and Pinard (Ibid. **31**: 226, 1911)	1911	Increased	Clear	40 lymphocytes per field	.....	Positive	.....
Gouget (Lecons de clinique medicale) 1911	1911	Marked increase	.....	83 cells per c.mm. (?)	.....	Not increased	.....
Mosny and Saint Girons (Bull. et mém. Soc. méd. d. hôp. de Paris **31**: 301, 1911)	1911	.....	.....	39 cells per c.mm., 97 per cent. lymphocytes	.....	.....	.....
Widal (J. des praticiens **26**: 228, 1912)	1912	Relief from headache by lumbar puncture	.....	Slight lymphocytosis	Increased	.....	.....
Leclerc, Pallase and Charvet (Lyon méd. **118**: 1044, 1912)	1912	(1) Increased	.....	Polymorphonuclears, 32.5 per cent.; large mononuclears, 17.5 per cent.; lymphocytes, 50 per cent.	.....	.....	.....
		(2) Pressure lessened as compared to first puncture		Polymorphonuclears, 34 per cent.; lymphocytes, 64 per cent.; large mononuclears, 2 per cent.	.....	.....	.....
De Massary and Vallery-Radot (Bull. et mém. Soc. méd. d. hôp. de Paris **33**: 85, 1912)	1912	Increased, escaping in a jet	.....	6.8 lymphocytes per c.mm.	.....	.....	.....
Plate (München. med. Wchnschr. **60**: 2343, 1913)	1913	440 mm. water	.....	258 cells, almost all lymphocytes; later 270 cells per c.mm. falling to 14 in about seven weeks	.....	.....	.....

Boveri (Riforma med. **29**: 844, 1913).....	1913	30-50 cm. (Kroenig)	.....	Cellular reaction slight compared to tabes	.....	Increased by Nonne and Noguchi tests	.....
Thomas and Blackfan (Am. J. Dis. Child. **8**: 377, 1914)	1914	High on first of four punctures	Clear	20 to 40 cells, mostly mononuclear....	.....	Noguchi test positive	Fehling's test positive
Strong (Arch. Pediat. **37**: 532, 1920).....	1920	(1) Slightly increased	Clear	Less than 10 cells, mostly polymorphonuclears	Positive	Positive	Positive
		(2) Normal	Clear	Less than 10 cells, mostly polymorphonuclears	Positive	Positive	Positive
		(3) Normal	Clear	Less than 20 cells, mostly polymorphonuclears	Positive	Positive	Positive
Barron and Habein (Am. J. M. Sc. **162**: 833, 1921).....	1921	Slightly increased	Clear	6 cells per c.mm.	.....	Nonne test negative	.....
Norton (Internat. Clin., Ser. 32, **4**: 231, 1922).....	1922	(1)	Clear, faintly yellow	12 cells per c.mm., 95 per cent. polymorphonuclear	.....	Positive (+)	Positive
		(2) Increased; recorded as +++	Clear	30 cells per c.mm.; polymorphonuclears, 3 per cent.; lymphocytes 27 per cent.	.....	Positive (++)	.....
Krafftczyk (Deutsch. Ztschr. f. Nervenh. **80**: 184, 1923)..	1923	(1) 165 mm. water	Clear	Slight lymphocytosis	Increased	.....	.....
		(2) 25 c.mm. water	Clear			Nonne 1 negative	.....
		(3) 100 mm. water	.....	No cellular elements.....	Trace	.....	.....
Suzuki and Kaneko (J. Oriental Med. **11**: 55, 1924)....	1924	(1) First pressure, 400 mm. water; second pressure, 200 mm. water	Clear	4 cells per c.mm.; polymorphonuclears, 2; small lymphocytes, 2	0.066 per cent.	Pandy positive; Noguchi positive; Nonne-Apelt, Phase I, positive	Haines' positive
		(2) First pressure, 400 mm. water; second pressure, 150 mm. water		20 cells per c.mm.; polymorphonuclears, 14; small lymphocytes, 6; later count: 48 white cells per c.mm.; polymorphonuclears, 30; small lymphocytes, 18; large lymphocytes, 0; 4 red blood cells	Increased	Positive	Positive

There is general agreement that the pressure of the cerebrospinal fluid is increased in lead meningo-encephalopathy. In several cases in which more than one puncture was made there is evidence that a high pressure was found early in the disease and that the pressure fell coincidentally with a clinical improvement following withdrawal and elimination of lead. Lacking information as to the technic employed in taking the pressure, the author's statement that the pressure was increased is of more significance than the numerical expression.

An increased cell count is found in practically all of the reported cases, but it becomes evident that the cytologic picture is not that of a simple lymphocytosis alone, for frequently a polymorphonuclear reaction of slight or moderate degree has been encountered in sterile fluids. The higher percentages of polymorphonuclears have been found in children, while most of the adult cases have shown a lymphocytosis of 60, 90 or even 97 per cent. It may be that those cases which are relatively acute, or in which a massive poisoning occurs, are more likely to show a greater number of polymorphonuclear cells. This point requires further illumination from clinical data.

The albumin increase of the earlier writers is substantiated by the positive globulin tests shown in practically all of the more recent cases. Boveri [12] states that in some fluids there is an increase in albumin and a decrease in cells. Such a dissociation of these two factors is not borne out by other observations.

Suzuki and Kaneko [1] have reported an increased sugar content in the cerebrospinal fluid of children showing this condition. All of the examples in which tests for sugar are given seem to be in accord with this view. In several cases we are given no information as to whether a pathologic increase is meant when a positive test is recorded, for a normal fluid gives a slight reduction. If further observations show an increased sugar content to be a constant finding in lead meningo-encephalitis, a new point of diagnostic importance will have been added.

While the Wassermann reaction has been negative in the reported cases, the older literature has frequently emphasized the apparently augmented meningeal reaction in cases in which syphilis and lead poisoning were simultaneous causal factors. It is beyond the scope of this paper to go into this interesting question. If true, as seems probable, we must expect a positive Wassermann test in a larger percentage of cases of lead meningo-encephalopathy than the laws of chance alone would demand. Lereboullet and Faure-Beaulieu [18] believed the Wassermann test to be more readily positive in syphilis plus lead poisoning than in syphilis alone.

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18. Lereboullet, P., and Faure-Beaulieu, M.: Le plomb et les centres nerveux, Paris méd. **7**:477-484, 1911-1912.

The clinical evidence at hand, therefore, gives as the important findings in the human cerebrospinal fluid in cases of lead poisoning with meningo-encephalopathy a moderately increased pressure; a clear, colorless or slightly yellow, sterile fluid; an increased cell count, often chiefly lymphocytic, sometimes polymorphonuclear; positive globulin tests; sugar present and probably increased.

AGREEMENT BETWEEN LABORATORY FINDINGS IN CLINICAL, AND HISTOPATHOLOGY OF EXPERIMENTAL, LEAD MENINGO-ENCEPHALOPATHY

If this question be approached from the experimental side, a number of interesting problems at once present themselves. One of these is whether or not there can be induced in experimental animals any histologic changes which would be compatible with the production of a cerebrospinal fluid of the type found clinically.

It is well known that in most laboratory animals signs of marked central nervous system involvement can be produced by the administration of lead. Epileptiform convulsions constitute the most striking manifestation. Such have been noted by Rosenstein,[19] McCarthy,[20] Catalano,[21] Sazuki and Kaneko [1] and others as occurring in dogs. In rabbits, convulsions rarely occur until the animal is about to die, when a single convulsion may close the picture. In guinea-pigs, as was noted by Popaw [22] in 1885, epileptiform convulsions, with both clonic and tonic phases can be produced with great constancy by the oral administration of lead compounds. The clinical picture of the convulsive type of human lead meningo-encephalopathy can be duplicated in these animals in a most striking fashion. Also after a convulsive seizure, a state of active confusion may persist. Such an animal has been noted as continuing to circle about its cage in an unseeing, aimless manner for hours at a time. Convulsions may be produced in guinea-pigs by a few relatively large doses of lead by mouth, or they may develop after a long period of time during which the administration of lead has been so carefully controlled that no marked loss of weight occurs.

No complete report on the general histopathology of the central nervous system of the animals in which we have produced an experi-

19. Rosenstein, S.: Ueber Epilepsia saturnina und ihre Beziehungen zur Urämie, Arch. f. path. Anat. **39**:1-14, 1867.

20. McCarthy, D. J.: Cerebral Lesions in Experimental Lead Intoxication, Univ. of Penn. Med. Bull. **14**:398-400, 1902.

21. Catalano, G.: Alterazion anatomo-pathologiche del sistema nervoso nell' avvelenamento sperimentale cronico da piombo, Policlinico Rome **13**:324-332, 1906.

22. Popaw, N.: Ueber die Veränderungen im Rückenmarke nach Vergiftung mit Arsen, Blei und Quecksilber, Arch. f. path. Anat. **93**:351-366, 1885.

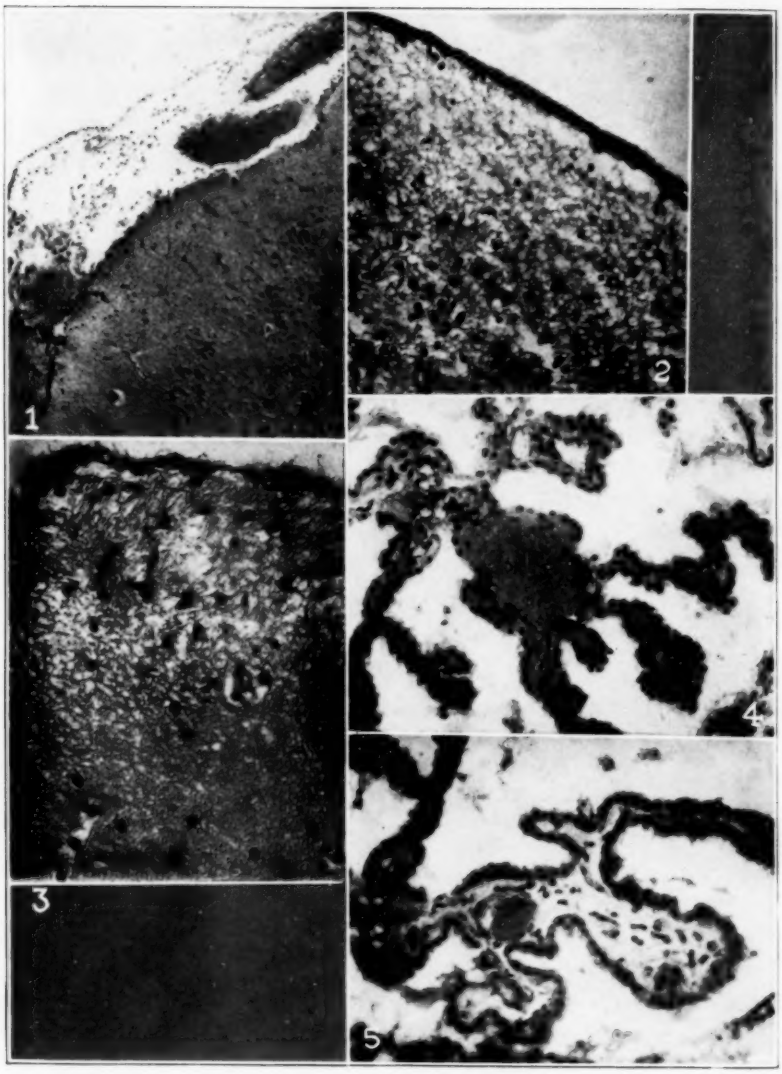

Fig. 1.—Marked meningeal congestion and edema, with moderate lymphocytic infiltration. This, and the four following photomicrographs, were made from guinea-pigs dying in convulsions after four doses of commercial white lead, given by mouth. (Hemalum and eosin stain; Zeiss objective B, no ocular.)

Fig. 2.—Extreme edema of the brain substance near a lateral ventricle with swelling and hydropic change of the ventricular ependyma. (Hemalum and cosin stain; Zeiss objective B, compensating occular No. 4.)

Fig. 3.—Extreme edema beneath the ventricular ependyma, with some swelling of the ependymal cells. (Hemalum and eosin stain; Zeiss objective B, compensating ocular No. 4.)

Fig. 4.—Choroid plexus with marked congestion and swelling of the ependymal cells, giving them a markedly hypertrophic appearance. (Hemalum and eosin stain; Zeiss objective B, compensating ocular No. 4.)

Fig. 5.—Congestion of the choroid plexus with marked edema in the villi shown in this field. Swelling of the ependymal cells. (Hemalum and eosin stain; Zeiss objective B, compensating ocular No. 4.)

mental lead meningo-encephalopathy can be made within the limits of this paper. We wish to call attention, however, to the fact that even in the most acute convulsive type of the disease there are changes which are in full accord with the human cerebrospinal fluid findings. As is shown in Figures 1 to 5, there is a venous congestion which is more marked in the pia and in the choroid plexus than in the brain substance; an extreme edema, most noticeable beneath the ventricular ependyma and in the inner meninges, and a slight and rather diffuse lymphocytic infiltration in the inner meninges, especially about the pons and cerebellum. The ependymal cells of the choroid plexus have a swollen appearance, which is shown by the parietal ependymal cells as well. The extreme edema of the brain substance gives areas of marked separation of the glial fibers approaching a liquefaction necrosis. The guinea-pigs from which the photomicrographs illustrating these changes were made had each received by mouth on successive days four doses of commercial white lead, 0.126 gm. to the average dose, administered in No. 5 gelatin capsules after being ground to a soft paste with starch and linseed oil, a method of administration which we have used in a variety of lead experiments during the past twelve years. These animals commenced to have convulsions on the fifth day, and died on the fifth to the eighth day after the first dose. The congestion, edema and swelling of ependymal cells are in accord with the increased pressure found clinically, and probably explain the increased globulin as well. The lymphocytic infiltrations fit with the lymphocytosis of the fluid. We found no evidence of a polymorphonuclear reaction. We wish to call attention to the absence of perivascular mantling such as is found in the so-called spontaneous encephalitis of rabbits. We have selected the guinea-pig to furnish the illustrative material because of the unfortunate confusion between spontaneous and experimentally produced rabbit encephalitis which has crept into the literature.

LEAD CONTENT OF CEREBROSPINAL FLUID

The alterations of the cerebrospinal fluid which are found in practically all of the cases of lead meningo-encephalopathy in which the fluid has been described are not such as to make a diagnosis of lead poisoning certain in and of themselves. While they should be of great value in eliminating certain other diagnoses and might confirm a suspected case, the possibility of an early tuberculous or syphilitic meningitis could not be excluded on such findings alone. Negative evidence by the Wassermann test or animal inoculation might help by exclusion, and knowledge of exposure to a lead hazard with the presence of a lead line or of chromatophilia and basophilic stippling of the red cells would practically establish the diagnosis. Lacking these, however, how valuable it would be if the diagnosis could be confirmed by the identification of lead

in the cerebrospinal fluid itself! Notwithstanding the general belief that most metallic substances do not pass through the choroid plexus or the meninges, it seems highly probable that lead must enter the fluid, although perhaps in exceedingly minute quantities.

Camus,[23] in experiments which have been largely ignored by recent writers, obtained evidence suggesting that the convulsions of lead meningo-encephalopathy might be due in some way to the presence of lead in the cerebrospinal fluid. He found that by injecting small amounts, 1 or 2 c.c., of a 1:500 solution of lead chlorid into the cerebrospinal fluid of a dog, he could produce, after a latent period of two or three days, restlessness, crises of agitation, the aspect of hallucinations and epileptiform convulsions, followed by semicoma and death in from twenty-four to forty-eight hours. These results were entirely like those produced when lead is given orally, or by either intravenous or subcutaneous injection. These results did not follow when the lead solution was injected into the parenchyma of the brain. Lead butyrate was used successfully in the spinal canal, showing that the effect was not due to the chlorin.

TABLE 2.—*Reported Examination of Cerebrospinal Fluid for Lead*

Date	Author	Procedure	Result
1907	Marie and Requier (Semaine med. **27**: 215, 1907).....	Not stated	Negative
1908	Bernard and Troisier (Bull. et mém. Soc. méd. de hôp. de Paris **25**: 484, 1908)	"Reaction sensitive to 1:100,000 or 1:200,000"	Negative
1908	Marie and Trillat (Ibid. **28**: 104, 1908).....	Method of Trillat	Positive
1910	Marie and Beaussart (La Clinique, Paris **5**: 117, 139, 1910)	Method of Trillat	Negative
1911	Gouget (Leçons de clinique medicale, 1911, p. 228)...	Method of Trillat	Positive
1920	Strong (Arch. Pediat. **37**: 532, 1920).....	Not stated	Negative
1923	Kraffeyzk (Deutsch. Ztschr. f. Nervenh. **80**: 184, 1923)	Not stated	Negative

Strong,[14] in 1920, failed to find lead in the cerebrospinal fluid of his case of lead meningitis. At that time he discussed the possibility of lead reaching the cerebrospinal fluid through increased permeability of the choroid plexus or other pathologic change. He wrote "but conclusions can only be reached by experimental work with lead." He apparently was not aware that there were already in the literature two reports claiming the successful demonstration of lead in the cerebrospinal fluid of patients showing a lead meningo-encephalopathy. In Table 2 are assembled all of the reported clinical examinations of the cerebrospinal fluid for lead which we have been able to discover in the literature. We have found no report of any experimental investigation of this point. Marie,[24] in 1908, gave the clinical history of a patient in whose cerebro-

23. Camus, J.: Toxicité des sels de plomb sur les centres nerveux. Leur période d'incubation, Compt. rend. Soc. de biol. **68**:509-511, 1910. Méningite et intoxication saturnine, ibid. **72**:861-864, 1912.

24. Marie, A.: Cerveau de paralytique général saturnin, Bull. et mém. Soc. méd. d. Hôp. **28**:104-107, 1908.

spinal fluid Trillat found the characteristic reaction of lead, but in an amount too small to permit quantitative estimation. The subject was a painter, 45 years old, who also had general paresis, having had syphilis twenty years before. Lead was subsequently demonstrated in the brain to the commuted amount of 4.435 gm., but with such a difference between the amounts in the two hemispheres as to raise some question. The method used on the cerebrospinal fluid was that known to the French as the procedure of Trillat. This consists (Heim, Agasse-Lafont and Feil [25]) in destruction of the organic matter followed by colorimetric estimation using basic tetramethyl diphenylmethane in acetic acid solution. This method is said to be sensitive to 0.00002 or 0.00001 mg.

The only other positive finding of lead in the cerebrospinal fluid was also obtained by the method of Trillat. This was reported by Gouget [26] in 1911, the estimation having been made by Hebert. Lead to the amount of 0.05 mg. was found in 14 c.c. of cerebrospinal fluid. The patient was a color maker working with lead pigments. He had had lead colic previously. One week after admission, he had an epileptiform crisis followed by seven or eight other seizures on the same day and more severe ones on the next. Lead to the amount of 0.03 mg. was recovered from 155 gm. of brain substance, an equivalent of 0.23 mg. for the entire brain.

Unless some mechanism exists by which a proportionately greater amount of lead reaches the cerebrospinal fluid, or by which it is retained and concentrated in the fluid, as compared to the parenchyma of the brain and cord, one can expect but minute amounts of lead to be present in it. Considering the facts that the cerebrospinal fluid is a changing, circulating medium, perhaps renewed several times in twenty-four hours, and that sometimes but a fraction of a milligram of lead can be found in the entire brain in a fatal case of lead poisoning, not much can be expected from a clinical specimen consisting of from 5 to 20 c.c. We know very little, however, not only about the rate of absorption of the cerebrospinal fluid, but also about the possibility of selective mechanisms being concerned. There is abundant evidence that lead becomes at least temporarily fixed in certain tissues and thereby withdrawn, in part, from the general circulation.

The work of the Harvard group on lead and of L. T. Fairhall,[27] in particular, has made it possible to do satisfactory qualitative tests for

25. Heim, F., Agasse-Lafont, E., Feil, A.: Contribution a l'étude du saturnisme professionel. Le dépistage, par les méthodes de laboratoire, du presaturnisme et du saturnisme confirmé, Le Bull. méd., Paris **36**:223-226, 1922.

26. Gouget, A.: Encéphalopathie saturnine. Leçons de clinique médicale, Paris, Masson et Cie., 1911, pp. 228-245.

27. Fairhall, L. T.: The Estimation of Minute Amounts of Lead in Biological Material, J. Ind. Hyg. **4**:9-20, 1922. Lead Studies. VIII. The Microchemical Detection of Lead, J. Biol. Chem. **57**:455-461, 1923.

exceedingly small amounts of lead present in relatively large quantities of biologic material. Results of chemical research on the body fluids and organs of cases of lead poisoning have formerly been notoriously inconsistent and uncertain. There can be but little doubt that much of the older work is without value. Lead has escaped detection, and other substances have been confused with lead, so that errors in both directions have occurred. From both quantitative and qualitative standpoints the newer methods are much superior. The successful prosecution of our present research has depended largely on the work of Fairhall [28] in refining the technic of the hexanitrite test for lead. Mott,[29] in 1909, had used this method on the brain from a case of chronic lead encephalitis, without success.

In endeavoring to demonstrate the passage of lead into the cerebrospinal fluid by experimental means, we found it necessary to use rabbits. The guinea-pig does not supply a sufficient amount of fluid, and it was inexpedient to use dogs at the time the work was being carried out. In many respects, the dog would be the animal of choice, but the rabbit has one advantage in that it withstands heavy doses of lead with but little probability of sudden death in convulsions. Lead was administered in some cases by subcutaneous injection of 1 per cent. acetate in varying amounts. To most of the animals lead was given by mouth in capsules containing a known amount of commercial white lead. Lead administration was continued from two days to two months before the animals were used. The fluid was obtained by killing the animal with chloroform, cutting down on the cervical vertebrae and withdrawing the cerebrospinal fluid with a fine hypodermic needle inserted somewhat to one side of the midline between the occiput and the first cervical vertebra, the point of the needle being directed somewhat mesially and kept close to the meninges. From 0.8 to 1.2 c.c. of clear fluid was usually obtained. Occasional contamination with blood occurred.

In our first attempts to demonstrate lead, we used fifteen rabbits. We employed Fairhall's [27] volumetric method, in which, after proper preparation of the unknown, the lead is precipitated as the sulphide, dissolved in nitric acid, reprecipitated as the chromate, filtered, dissolved in hydrochloric acid, excess of potassium iodid added, and the liberated iodin titrated with sodium thiosulphate. In our work we are unable to differentiate, by this method, between the cerebrospinal fluid of our lead treated rabbits and that of normal rabbits. We were forced to conclude that either lead did not reach the cerebrospinal fluid at all or was not present in sufficient amount to respond to the test. Fairhall advised

28. Fairhall, L. T.: J. Biol. Chem. **57**:455-461, 1923.

29. Mott, F. W.: Examination of the Nervous System in a Case of Chronic Lead Encephalitis, Arch. Neurol. & Psychiat. **4**:117-130, 1909.

against the use of this method for amounts of 0.05 mg. of lead, or less. After thorough trial, this method was therefore abandoned.

We next turned to the most successful microchemical test for lead, the hexanitrite test. Although looked on as uncertain by most chemists who had worked with it, Fairhall [28] had apparently produced a promising standardized technic. In the second period of our research, we made use of Fairhall's method, except that we used the more sensitive cesium salt to replace the potassium in the hexanitrite crystals and did not precipitate as the sulphide with added copper to entrain the lead. We hoped that the precipitation step would not be necessary in view of the small amount of inorganic material present in the cerebrospinal fluid.

Using the known solution directly on a slide, we found that a satisfactory test for lead could be obtained from 0.5 mg. (00.000005 gm.) of lead acetate, and a positive test, the crystals being found with some difficulty, with as little as 0.2 mg.

Four rabbits treated with lead gave positive lead tests in the cerebrospinal fluid, but we then found a few hexanitrite crystals from the fluid of a normal rabbit, indicating contamination. This source of extraneous lead was finally determined to be in the potassium nitrite. After repurification of this and substitution of nitric acid which had been redistilled, no further difficulty was experienced from positive tests in control material. The four positive findings could not be accepted as proof of the passage of lead, although they revealed a larger amount of lead than was shown by the false positive in the control rabbit.

Eight additional animals were utilized after substituting the recrystallized potassium nitrite. Of these, one only gave a strong positive test. The negative findings in the others served as an effective control of reagents and glassware used. A careful review of the experiment revealed no known opportunity for contamination in the positive case, and this result was allowed to stand as a true positive.

Through the cooperation of Dr. C. D. Camp of the University Hospital and of Dr. A. M. Barrett of the State Psychopathic Hospital we were provided with human cerebrospinal fluid. That from two patients, whose history led us to believe that lead poisoning might be present, failed to show lead by the method we were then using. Likewise, when minute quantities of lead were added to normal fluids and these were incubated for several hours in the hope of simulating the organic binding of the lead as it occurs in the body, we found that the lead could not be demonstrated consistently. The inorganic material interfered so seriously with the test as to invalidate it. When, however, we used the Fairhall [28] method of concentrating the lead by precipitating it as a sulphide together with a certain amount of copper, centrifugating and washing the precipitate, and then redissolving and carrying out the hexanitrite test, we found no difficulty in demonstrating 0.000001

gm. of lead acetate added to 5 c.c. of human cerebrospinal fluid. So abundant were the crystals formed from one half of the residue in this instance that there is no doubt that with this modification the test would prove positive for quantities considerably smaller than the one stated, approximating the lower limit for a positive test with lead acetate dissolved in water alone.

Since adopting our final procedure, which seems to have overcome all of the difficulties from the chemical side, we have had positive results for lead from the cerebrospinal fluids of three additional rabbits to which four and five capsules of commercial white lead, averaging 0.86 gm., had been administered by mouth. In two of these fluids there was a trace of blood, shown by a faint pinkish tint when viewed by white light. We do not know whether this represented a technical contamination or a slight hemorrhagic exudation. Such red blood cells as were present were removed by centrifugation before chemical analysis. The presence of blood plasma would lessen the value of these two examples as used to prove the transmission of lead into the cerebrospinal fluid. In the third instance, there were no circumstances which would lead us to question its validity.

We believe that we have demonstrated the transmission of lead, administered by mouth, to the cerebrospinal fluid. However, we wish to make only a preliminary report on this point at this time, reserving final judgment until a further series of animals can be tested. We believe that the procedure outlined below provides the chemical means for carrying out this test in animals and in the cerebrospinal fluid of patients thought to have lead meningo-encephalopathy. We anticipate that certain of the organic compounds of lead may be found to enter the cerebrospinal fluid with greater ease than when lead is inspired or ingested in inorganic form. There seems to be a marked difference in individual animals as to the extent to which lead enters. This may be due to varying conditions affecting absorption from the gastro-intestinal tract.

ADAPTATION OF HEXANITRITE TEST STANDARDIZED BY FAIRHALL TO EXAMINATION OF HUMAN CEREBROSPINAL FLUID

Procedure.—(1) The available cerebrospinal fluid is evaporated to dryness in a small Kjeldahl flask. (2) The organic matter is decomposed by the addition of 5 c.c. of nitric acid added 1 c.c. at a time. More acid may be needed to effect decolorization. Finally, from 0.5 to 1 c.c. of sulphuric acid is added and heating is continued until no more fumes are evolved. (3) The residue is dissolved completely in hydrochloric acid, using from 1 to 2 c.c., and washed into a test tube holding at least 20 c.c. (4) Strong sodium hydroxid solution is used for neutralization, and hydrochloric acid makes it slightly acid to methyl orange. (5) One cubic centimeter of saturated ammonium sulphate is added and from 1 to 2 drops of 2 per cent. copper acetate. (6) Precipitation is then caused by saturation with

hydrogen sulphid, and the precipitate is concentrated in one centrifuge tube by centrifugating and decanting the supernatant liquid. (7) The precipitate is washed in the same tube at least three times, the water being drained from the precipitate after each centrifugation. (8) After the final washing, from 2 to 3 drops of nitric acid is added to the precipitate in the centrifuge tube, and the tube is placed in a beaker of boiling water until the precipitate is dissolved. (9) The resulting solution is drawn up in a capillary tube and evaporated to dryness on a microscopic slide, the area being kept small by the application of one drop at a time.

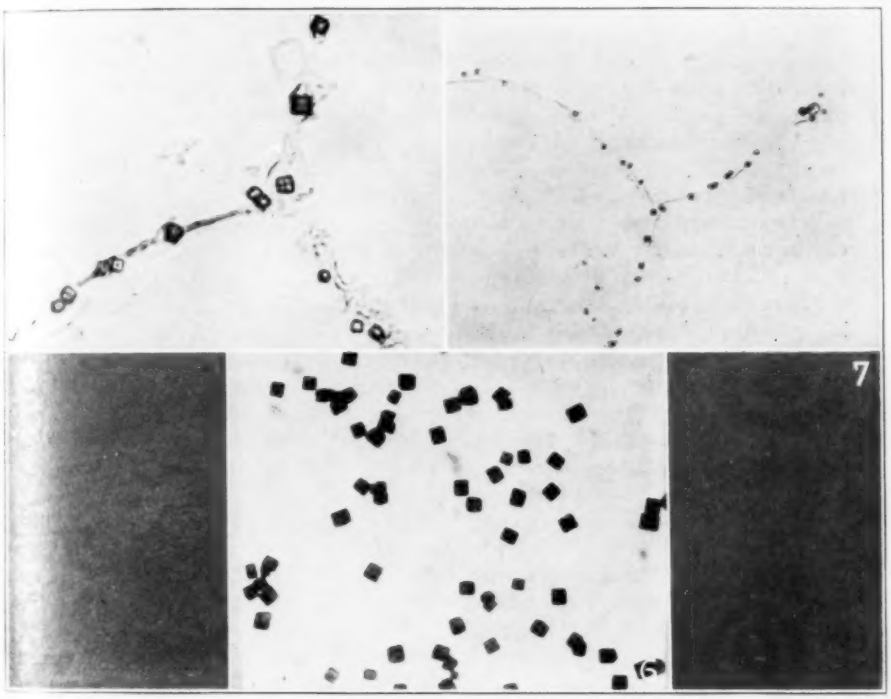

Fig. 6.—The hexanitrite crystals of eosium, copper and lead as prepared from a dilute solution of a pure lead salt. Note the uniformity of outline. (Balsam mount after drying; Zeiss objective B, compensating ocular No. 4.)

Fig. 7.—Characteristic lead crystals (hexanitrite) as prepared from 5 c.c. of human cerebrospinal fluid to which 1 microgram (0.000001 gm.) of lead acetate had been added. Note the grouping of the crystals along residual material. (Zeiss objective B, compensating ocular No. 4.)

Fig. 8.—A high power view of isolated crystals from the same preparation. The photographic plate reveals the refractive properties of these crystals. In shape they are still characteristic in spite of their small size. (Zeiss objective DD, compensating ocular No. 4.)

(10) From 5 to 10 c.mm. of 4 per cent. sodium acetate solution is added, mixing with a glass needle to dissolve all the residue but taking care not to enlarge greatly the area of the fluid on the slide. (11) The fluid is evaporated to dryness on the slide and chilled on ice. (12) Five cubic millimeters of 10 per cent. acetic acid is added and a small crystal of potassium nitrite and a small crystal of

cesium chlorid are placed centrally. (13) It is then covered with a cover glass and examined with the high dry lens (4 mm.).

The presence of lead is shown by the highly characteristic crystals of the hexanitrite ($CsCuPb[NO_2]_6$). These crystals are small yellowish-red to brownish-black square plates and cubes. The color is dependent on the thickness of the particular crystal. A few oblong forms will be found in examining a large number of crystals, as well as a few which appear unequally hexagonal. The latter are cubical or nearly cubical crystals so poised as to present an angle toward the observer. In size, the crystals vary from those just capable of being resolved as squares with the high power of the microscope up to about 20 microns in diameter. They are highly characteristic, and in examining many slides we have found no other crystalline structure with which they might be confused. Although averaging smaller than those made with the potassium salt, the cesium crystals show much less variation in form, and their smallness is an advantage in that they appear brighter red. Since the addition of cesium renders the method about five times as sensitive as when potassium is used, we recommend it for the examination of the spinal fluid for lead.

The small amounts of sodium acetate solution and of dilute acetic acid required can be conveniently measured in routine work by calibrating home-made capillary pipets. Such pipets can be made to deliver a droplet of about 5 c.mm. volume.

The entire test should be run through in blank as a control. Any difficulty may be due to the potassium nitrite, the nitric acid or the utensils used. Fairhall [28] gives the following satisfactory method for the purification of potassium nitrite.

"Silver nitrate should be added to the filtered solution of potassium nitrite and the resulting precipitate of silver nitrite washed well with cold water. This silver nitrite is then dissolved in boiling water and an equivalent amount of pure potassium chloride added. The pure potassium nitrite in solution may then be crystallized by evaporating this solution to a small bulk."

The nitric acid may be freed from lead by redistilling, preferably from a silica flask. It is all allowed to lie for at least twenty-four hours in nitric acid and washed in distilled water before being used. We have used Pyrex glass, Kjeldahl flasks of 50 c.c. capacity, and have had no evidence that lead was derived from our laboratory glassware.

While this method may at first seem rather formidable, once one is assured of proper reagents it offers no serious difficulties. It can be performed by any one accustomed to such laboratory procedures as the Wassermann test and routine blood counting, and the entire method can be carried out in one and one-half hours.

SUMMARY

In this paper, by combining material derived from historical, clinical and experimental fields, we have endeavored to develop a definite conception of the cerebrospinal fluid in lead meningo-encephalopathy. We have shown by selected references from the literature the gradual separation from the group of lead encephalopathy of a subgroup in which evidence of meningeal involvement plays an important part. The cerebrospinal fluid findings of this group have been summarized and found to be fairly constant, but not in themselves diagnostic. The value of the recognition of lead in the fluid itself, if it occurs there, at once becomes evident. Its successful recognition has twice been reported. Since administration of lead to laboratory animals by various methods,

including injection into the spinal canal, produces a clinical condition comparable to human lead meningo-encephalopathy, with histologic changes in accordance with the findings in the cerebrospinal fluid of human cases, experimental investigation of the fluid of animals is justified. Having, we believe, successfully demonstrated the passage of lead into the cerebrospinal fluid of lead poisoned rabbits by means of Fairhall's modification of the hexanitrite test, we have arranged an adaptation of this test suitable for the clinical laboratory examination of cerebrospinal fluid. If it is found that lead is transmitted to the fluid in human cases as it seems to be in the rabbit, this method should prove of great diagnostic value.

CONCLUSIONS

1. The cerebrospinal fluid in lead meningo-encephalopathy is a clear sterile fluid showing increased pressure, an increased number of cells —more commonly mononuclears, though sometimes polymorphonuclears—increased globulin content and probably increased sugar. Twice the recognition of lead in the cerebrospinal fluid has been reported in the literature.

2. In guinea-pigs dying with clonic and tonic convulsions after ingestion of lead, the histologic changes in the choroid plexus, ependyma, brain substance and meninges are such as to be in accord with the cerebrospinal fluid changes found in human cases.

3. We believe that by the improved hexanitrite test (Fairhall) we have successfully demonstrated the passage of lead into the cerebrospinal fluid of lead poisoned rabbits. This point requires further verification and will be the subject of a later report. There appears to be much variation in this respect among different animals receiving the same dosage.

4. We suggest that this test be used to ascertain whether a similar transmission of lead occurs in human lead meningo-encephalopathy, and we recommend its adoption as a diagnostic procedure if such should be found to be the case.

INTRACRANIAL DERMOID CYSTS

REPORT OF A CASE, WITH OPERATIVE FINDINGS

CARL WHEELER RAND, M.D.

LOS ANGELES

Intracranial cysts of the dermoid type are seldom recognized clinically. It is doubtful whether any case of dermoid cyst of the brain has been diagnosed before operation. Occasionally one has been revealed at the operating table, but most of the cases have been reported from necropsy material. The presence of a crescentic shadow in roentgenograms, caused by a calcified area in the wall of the cyst, has been observed in two or three instances. The finding of similar shadows in cases of suspected brain tumor, while not pathognomonic, should at least suggest the possibility of a dermoid cyst. The whole subject of intracranial dermoid and epidermoid cysts, cholesteatomas and teratomas has become considerably confused in nomenclature, as the nature of the lesion depends not only on the cell layers from which these growths arise—be they epithelial or endothelial in origin—but also on the location and the nature of the contents of the central mass. Teratomas and cholesteatomas of otitic or choroid plexus origin are not considered in this report.

Certain of these growths—usually cystic—are now recognized because of the well-known pearly luster of their capsule. They seldom, though sometimes, contain hair, and usually, though not always, contain cholesterin crystals. Their growth is exceedingly slow, and they probably arise from an epithelial cell "rest" made up of the cells normally found only in the outer layer of the dermis. Their point of origin is usually in the deeper structures of the brain near the midline, in the region of the hypophysis, from the remains of Rathke's pouch, or in the third or fourth ventricle, from which region they may invade the cerebellopontile angle.

Attention to the characteristic mother-of-pearl appearance of these tumors was perhaps first drawn by Duméril,[1] this being emphasized later by Cruveilhier,[2] who designated them "tumeurs perlées." Johannes Müller [3] gave them the name cholesteatoma because cholesterin crystals were found in several specimens described by him, but Virchow [4] later

1. Duméril: Bull. Soc. fac. de méd., Feb. 19, 1807.

2. Cruveilhier: Anat. pathol. du corps humaine, 1829, vol. 1, Book 2, Plate 6.

3. Müller: Ueber den feineren Bau und die Formen der krankhaften Geschwülste, 1838.

4. Virchow: Ueber Perlgeschwülste, Arch. f. path. Anat. **8**:371-418, 1855.

returned to the earlier terminology of pearly tumor. A recent careful search of the literature made by Bailey [5] has resulted in the finding of sixty cases of pearly tumor. To this number he has added two which were removed at operation by Cushing. The first of these occupied the fourth ventricle, and the second one was located in the third. Since then Cushing [6] himself has added another case of "a large extradural epidermoid cholesteatoma of the parieto-temporal region" occurring on the left side, which he successfully removed at operation. This, like the two reported by Bailey,[5] was of the nonhair-containing variety, and, like the second, contained cholesterin crystals in abundance. The first of the two cases reported by Bailey did not contain cholesterin crystals.

Cushing [6] believes that these extradural pearly tumors originate between the two layers of the skull in the diploetic spaces. As they grow, the tables of the skull are pushed apart with absorption of either the inner or outer table, or of both. As a rule, the inner table suffers more, and a fairly characteristic picture is shown in roentgenograms of the skull which will be referred to later. He has given brief abstracts of the reports of this type of case by Esmarch [7] who, in 1856, probably performed the first operation on such a tumor; he also mentions other cases reported by Weinlechner,[8] Wotruba,[9] Blecher,[10] Borchardt,[11], Koerner [12] and others.

The hair-containing variety of cholesteatoma, while described earlier by Veratus [13] than any of the epidemoid types above referred to, is apparently less frequent in occurrence. Horrax [14] has summed up the incidence of this more truly dermoid type. He suggests the term

5. Bailey: Cruveilhier's "Tumeurs Perlées," Surg., Gynec. & Obst. **31**:390-401 (Oct.) 1920.

6. Cushing: A Large Epidermal Cholesteatoma of the Parieto-Temporal Region Deforming the Left Hemisphere Without Cerebral Symptoms, Surg., Gynec. & Obst. **34**:557-566 (May) 1922.

7. Esmarch: Cholesteatoma im Stirnbein, Virchow's Arch. f. path. Anat. **10**:307-316, 1856.

8. Weinlechner: Wein. klin. Wchnschr. Feb. 14, 1889, No. 7, p. 136.

9. Wotruba: Ueber ein Cholesteatom im Stirnbein, Wien. klin. Wchnschr., Nov. 21, 1889, p. 889.

10. Blecher: Ueber Cholesteatome (Epidermoide) der Schaedelknochen, Deutsch. Ztschr. f. Chir. **70**:352-362, 1903.

11. Borchardt: Cholesteatom der hinteren Schaedelgrube, Arch. f. klin. Chir. **77**:892-899, 1905.

12. Koerner: Ein Cholesteatoma verum in der hinteren Schaedelgrube, Ztschr. f. Ohrenheilk. **37**:352, 1900.

13. Veratus: De Bononiensi scientiarum et artium instituto atque academia commentarri **2**: Pt. 1, 184, 1745.

14. Horrax: A Consideration of the Dermal Versus the Epidermal Cholesteatomas Having Their Attachment in the Cerebral Envelopes, Arch. Neurol. & Psychiat. **8**:265-285 (Sept) 1922.

"meningeal cholesteatomas" to cover that class of tumors "either hair-containing or otherwise" which have their attachment to the meninges. He has found twenty-six examples of the dermoid type. Eighteen were reported by Bostroem [15] and one each by Tannenhain [16] Trachtenberg,[17] Schlugin,[18] Teutschlaender [19] and Stanojevitz [20] and three more are added from Cushing's clinic. Of this entire series, he has mentioned only three which occurred in the middle fossa compressing the temporal lobe, i. e., one by Bostroem, one by Teutschlaender and one by Cushing. Curiously enough, all of these occurred on the left side, as did also the one being reported. The latter, however, is an extradural hair-containing dermoid, while apparently the other three were deeply embedded in the substance of the temporal lobe. The outstanding characteristic of these three cases seems to be the hour-glass form of the growth, the larger portion occupying the deeper structures of the temporal lobe and the smaller component being lateral in position. These tumors all contained hair, and the first two cholesterin crystals. The cases of Bostroem [15] and Teutschlaender [19] were disclosed at necropsy, while that reported by Horrax was found at operation. In his patient, two stages were required for its final removal, as the larger mesial portion, containing a calcified area in the cyst wall, was not found at the first exploration. Its entire extirpation was apparently accomplished at the second stage, as the patient was reported well nearly a year later.

Roentgenograms of the skull in two of the cases from Cushing's clinic are interesting and of diagnostic value. The case in which there was a large extradural epidermoid cyst showed a definite thinning of the vault in the left parietal region owing to the marked erosion of the inner and outer tables. There was a fairly clear line of demarcation caused by a ridge of the bone which formed a rim around the margin of the growth. In one of the cases reported by Horrax, a peculiar crescentic shadow was revealed on stereoscopic plates which appeared to be "above and to the left of the sella turcica." This shadow still persisted after the

15. Bostroem: Ueber die pialen Epidermoide, Dermoide und Lipome, und duralen Dermoide, Centralbl. f. allg. Path. u. path. Anat. **8**:1-98, 1897.

16. Tannenhain: Dermoid Cyste des dritten Gehirnventrikels, Wien. klin. Wchnschr. 1897, p. 494.

17. Trachtenberg: Ein Beitrag zur Lehre von den arachnoidealen Epidermoiden und Dermoiden des Hirns und Rückenmarks, Arch. f. path. Anat. **154**:274-291, 1898.

18. Schlugin: Zwei Fälle von Cholesteatom des 4 Ventrikels, Sowrem. Psichiat, Moscow, 1911, No. 1, p. 143.

19. Teutschlaender: Zwei seltenere tumorartige Bildungen der Gehirnbasis, Arch. f. path. Anat. **218**:224-248, 1914.

20. Stanojevitz: Mannfaustgrosses, lange Zeit hindurch ohne objective Symptome bestehendes und plötzlich zum Tode führendes klein Hirnteratom, Neurol. Centralbl. **37**:784, 1918.

first exploration. Following the second procedure, however, when a "calcareous shell" was removed with the lining membrane of the mesial portion of the cyst, further roentgenograms failed to reveal this shadow. Especial attention is called to these findings, as it would seem that roentgenologic examination of the skull may have definite diagnostic value in these rare cases. In my case, a somewhat similar shadow appeared in the left temporal fossa, which did not correspond exactly with either of the two cases just reviewed, but which undoubtedly had a definite relation to the wall of the cyst.

CASE REPORT

History.—N. M., a married woman, aged 40, who was referred by Dr. Josephine Jackson of Pasadena, came under observation on Nov. 6, 1922. She was complaining of headache, failing vision and "jerky spells." Her family history was unimportant. She had never received a head injury severe enough to render her unconscious. She had had no previous serious illness, although she had contracted pelvic inflammatory disease about fifteen years before. The onset of her present illness was insidious. About twelve years ago, she passed through a period of two and a half years of headache associated with nausea and vomiting, which she described as "sick headache." This condition gradually disappeared, and a relatively free period of several years followed. During the past three or four years, she had had recurring increasing discomfort in her head. For the past six months, she had noticed that the "left side of the head feels different from the right," the pain being localized in the temporal region. The headaches, not now associated with nausea and vomiting, had been increasingly severe and were practically constant. For the past two years, she had been aware of failing vision. A little more than a year ago, she consulted an ophthalmologist, who discovered double optic neuritis with elevation of about 2 diopters in the left eye and 1 diopter in the right eye. In charting her visual fields, he found a large central blind spot on the left side. She was fitted with glasses and instructed to rest. She continued studying, and her vision gradually but steadily grew worse. When first seen, she was practically blind in the left eye, although she could tell light from dark. The vision in the right eye was much below normal, with a tendency toward a temporal hemianopsia. She complained of blind spells in the right eye which were momentary, but which were increasing in frequency and duration. For the past few months, she had also had several "spells" during which her hands and feet would jerk. These spells are described as unsteadiness or shaking of the extremities rather than as true convulsions. Nothing of a definitely focal nature was elicited in these attacks. She also complained at times of a disagreeable taste in her mouth accompanied by a queer odor which she could neither account for nor describe. During the past six months she had had periods when she could not think of the right word, although she knew what she wanted to say and what was said to her.

Examination.—This revealed a well developed and well nourished woman of 40 years, with negative general physical findings. She was suffering considerably from headache, which was located in the left temporofrontal region. There was some tenderness over the left temporal region, where, on palpation, one had an indefinite sense of fulness.

Neurologic Findings.—The pupils were wide, regular and reacted to light and to accommodation. At times, the left pupil was larger than the right. Extra-ocular movements were normal. The eyegrounds revealed a marked choked disk of 4 to 5 diopters swelling, apparently of long standing. The veins were tortuous and deeply embedded. The disk structures were entirely wiped out; the optic cup was not seen; there were no hemorrhages or exudates, but a large amount of new tissue was present. The process was rather more marked on the left side. There was a zone of hyperesthesia in the region supplied by the ophthalmic division of the left trigeminal nerve. This region was more sensitive to touch, pain and temperature than elsewhere. The second and third divisions of this nerve, together with its motor component, were normal. There was possibly slight lagging of the left corner of the mouth. The patient had complained somewhat of tinnitus in both ears, but her hearing was good, and the tuning fork tests were normal. The cranial nerves were otherwise negative. Her mentality was unimpaired. The vision in the left eye could not be tested. In the right eye, on rough tests, there was definite constriction in all quadrants, more marked in the upper and lower temporal fields.

Laboratory Findings.—The spinal fluid was under somewhat increased pressure, revealing one cell in three fields. The Wassermann reaction was negative, and the butyric acid plus minus. Blood examination revealed: hemoglobin, 60 per cent.; color index, 0.8; red blood cells, 3,690,000; white blood cells, 10,800; blood Wassermann test, negative. Urinalysis revealed: color, yellow; reaction, acid; specific gravity, 1.010; albumin, trace; sugar, none; acetone and diacetic acid, none; an occasional hyaline cast; many epithelial cells, a few pus cells and an occasional red blood cell.

Radiographic Examination.—Dr. Carl H. Parker, of Pasadena, reported as follows on Nov. 3, 1922. A single anteroposterior view and stereoscopic views in both the right and left lateral positions were taken. In the lateral views (Fig. 1), the inferior and posterior walls of the sella turcica and the posterior clinoid processes could not be seen. The anterior clinoid processes showed distinctly. The curve of the body of the sphenoid, posterior to the sella, could also be seen. A peculiar semicircular calcification was noted in the left temporal fossa. This shadow had somewhat the shape of an enlarged and thickened sella turcica, although I do not believe that it had anything to do with the sella, because in position, it appeared to be in contact with the left wall of the skull. In width, this shadow was 3 mm., and the curve from below upward and backward measured 2 to 3 cm. Above and to the right, the calcification shaded off gradually, suggesting an elliptical or spherical body, which was partially calcified. In the postero-anterior view, the abnormal calcification appeared above the projection of the left mastoid. Its outline in this direction did not appear very clear because of the superimposition of other bodies.

Diagnosis.—A diagnosis was made of brain tumor, which was considered pituitary in origin, extending to the left across the base of the skull in the middle fossa and invading the temporal lobe.

First Operation.—On Nov. 11, 1922, a left osteoplastic flap was turned down. The skull itself was exceedingly thin in the upper parietal region but much thicker in the occipital and frontal regions. There was marked convolutional atrophy of the inner table of the skull. The temporal bone was found to be as thin as paper and at one point seemed eroded through. As the operator rongeured away part of the temporal bone at the base of the flap for better exposure, he unexpectedly encountered a point where a gummy, cheeselike mate-

rial exuded from the spaces between the inner table of the skull and the external surface of the dura. This substance was removed piecemeal with a curet and contained many fine dark hairs. It was of the consistency of cottage cheese, yellowish gray and was later shown to contain cholesterin crystals. About 80 cm. of this material was removed. The size of the cavity occupied by this mass was found to extend 5 cm. deep from the surface and about 6 cm. anteroposteriorly. It was irregular in outline, and the inner surface of the wall appeared to be a dull grayish white and of velvety texture. Fine hairs could be seen growing from the wall. The floor of the skull was rough and irregular, and at one point the petrous portion of the temporal bone was soft and worm-

Fig. 1.—Lateral view of skull. The crescentic shadow caused by partial calcification of the cyst wall is indicated by arrows. In stereoscopic examination this shadow lay near the inner table of the skull on the left side.

eaten. A search made for an opening into the mastoid region failed to reveal any direct communication. The capsule of this tumor was adherent to the dura itself, and it was deemed unwise to attempt its removal. After cleaning the cavity, the wound was closed. A dermoid cyst was diagnosed.

Following operation, the patient showed immediate improvement. The headache disappeared, and the vision in both eyes improved. Three days after operation, she could count fingers with the left eye and could read letters about 1 inch tall when held close to her eyes. The visual fields in the right eye increased, and by rough tests one could scarcely elicit any constriction. In about five days, the wound began to bulge along the anterior pole of the incision,

and on the tenth day a sinus developed. A thin, greenish material containing small bodies which looked like rice discharged for a period of weeks, and gradually the anterior portion of the bone flap became elevated. The disks showed decided improvement, with beginning emergence of the temporal margins. Two months after operation, the choked disk had subsided, until there was no measurable elevation, although there was still much new tissue and the disks themselves appeared pale. Form charts of the visual fields made from time to time showed the maximum improvement on Jan. 9, 1923 (Fig. 2).

About Feb. 1, 1923, the patient again began to experience fulness in the head with pain in the left temporal region. The fundi showed recurrence of pressure with indistinct disk margins and overfilling of the veins. They became elevated to about 2 diopters. The wound had continued to drain. On Feb. 9,

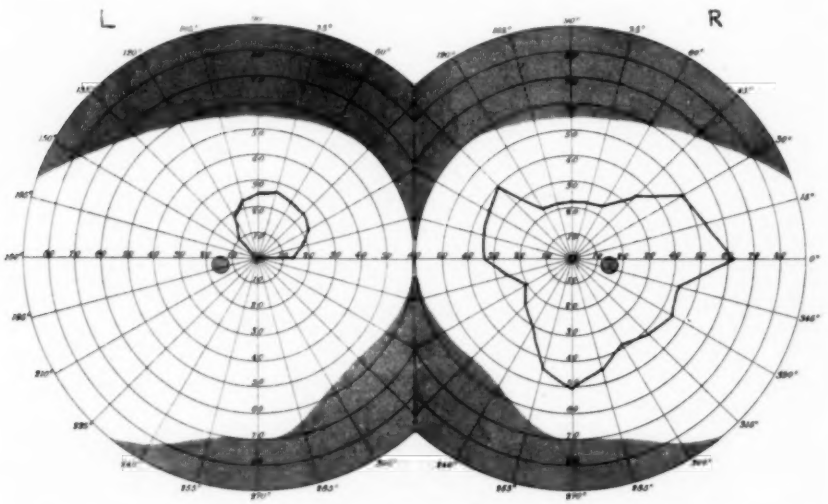

Fig. 2.—Form fields taken Jan. 23, 1923, two and a half months after the first operation; 5 mm. disk. Vision in the right eye was 20/50 plus; in the left eye, 20/200 minus.

1923, the visual field in the right eye had contracted markedly (Fig. 3). It was impossible to make a chart of the left field.

On Feb. 10, 1923, the wound was reopened, and dense adhesions were encountered at the base of the flap in the temporal region. After some difficulty, the operator succeeded in coming down to the old opening in the wall of the cyst. The cavity was filled with a dirty, brownish, cheesy material, which was semifluid and contained many particles resembling rice bodies. This was scooped out, and the opening in the cyst was enlarged until its entire cavity could be seen. Some hard débris which had been overlooked at the former operation was then removed from the anterior part of the cyst wall in the region of the optic chiasm. An attempt was made to dissect the wall from the floor of the skull, which was partially successful, but which was abandoned after the middle meningeal artery had been torn. An attempt to dissect the cyst wall from the under surface of the dura was also unsuccessful. After cleansing the cavity thoroughly and curetting the wall, the entire lining of the

cyst was painted several times with a strong Zenker solution. The wall at once took on the appearance of tissue that has been burned with silver nitrate. A folded gutta percha drain was then placed deep in the cavity and brought out at the base through the temporal muscle.

Pathologic Findings.—Dr. R. W. Hammack, Los Angeles, reported as follows: Wall of the cyst from the cranial cavity (Fig. 4); A small fragment of tissue was found in a mass of coarse, greasy material, containing fine hairs and cholesterin crystals. Microscopic examination of tissue revealed a thin layer of fibrous connective tissue covered on one side by stratified squamous epithelium. The epithelium varied in thickness but usually was thin. There were frequent long epithelial pegs extending into the connective tissue, but there was no evidence of malignancy. The horny layer was thin, and desquamated cells were seen. In the fibrous wall were a few areas of round cell infiltration sometimes containing giant cells of irritative type. There were lines of cleavage in the connective tissue suggesting the presence of crystals of some type. The diagnosis was dermoid cyst.

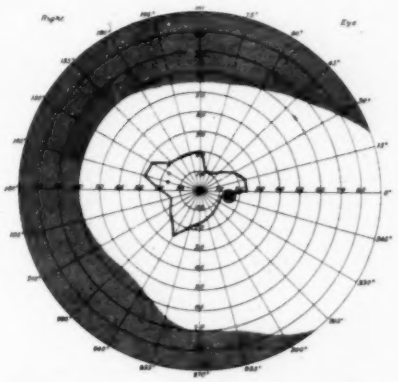

Fig. 3.—Form field taken Feb. 9, 1923, four days before the second operation; 5 mm. disk. Note marked contraction of right field. Vision in the right eye was 20/70 plus; the left eye could not be tested and the field could not be charted.

Course of Illness After Operation.—Following operation, there was transient numbness and weakness of the right arm, which lasted one day. The drain was removed at the end of ten days. During this period, spinal fluid drained copiously. Following removal of the drain, the spinal fluid leak stopped, but the sinus reopened later. The vision again improved, the maximum being reached about April 11, 1923 (Fig. 5). During the period of improvement, the fundi receded so that the temporal margins were clear-cut, although the nasal margins were still hazy; the veins were less full. Both disks were paler than normal. The patient was free from headache. A small amount of drainage persisted, which consisted of débris from the broken-down infected wall of the cyst. About the middle of April, she again began to experience fulness in the head, and vision became blurred in the right eye. The field was beginning to contract rapidly (Fig. 6). The margins of the disk were definitely more hazy than at last examination. The veins were full, and there was an elevation of about 1 to 2 diopters in each eye. Further operative procedure was advised.

Second Operation and Course of Illness.—On April 26, 1923, the bone flap was turned down, and the cyst was found without difficulty. It had become entirely filled with a grumous, cheesy material containing many fine hairs. After emptying the cyst of its contents, the operator decided to attempt its entire removal. It was necessary to sacrifice the dura from the under surface of the left frontal and temporal lobe in this procedure. The entire upper part of the cyst wall was excised, together with the dura. The remaining fragments on the floor of the skull were also removed. The cavity was then thoroughly

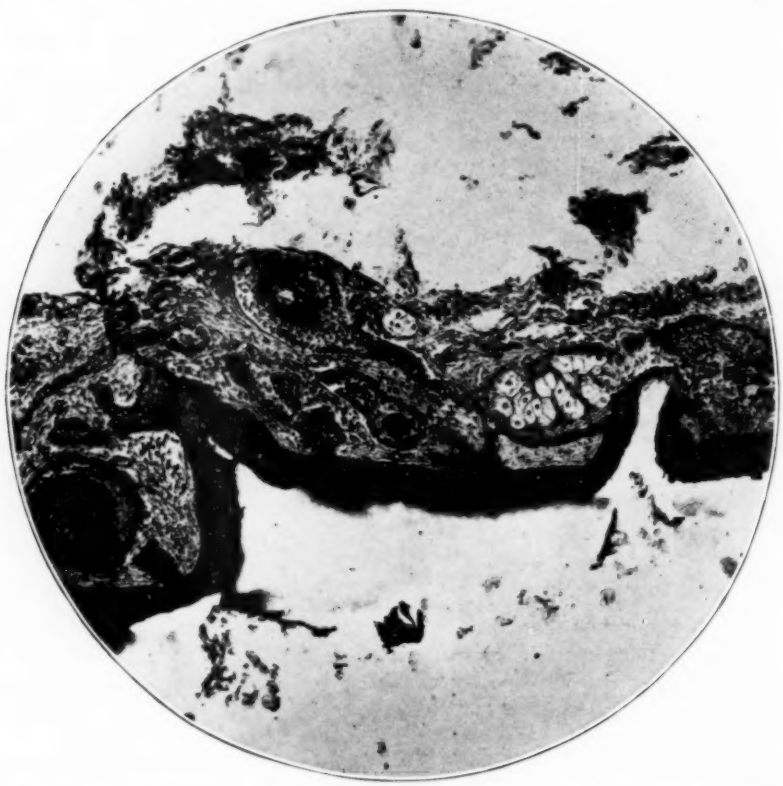

Fig. 4.—Photomicrograph of wall of cyst. Note practically all elements of true dermis and epidermis; i. e., hair follicles, sweat glands, stratified epithelium, etc. The desquamation of the horny layer is shown.

flushed with a warm salt solution. On closure a folded gutta percha drain was placed along the floor of the middle fossa and brought out at the anterior pole of the incision.

Following this procedure, improvement in vision again occurred. At the end of three days, she could count the fingers with the left eye, and the field in the right eye had returned to normal, as far as could be judged by rough tests. On the third day, the drain was removed. On the night of the fourth day, the patient developed a cerebrospinal rhinorrhea which persisted for twenty-four hours. This was immediately followed by a rise in temperature

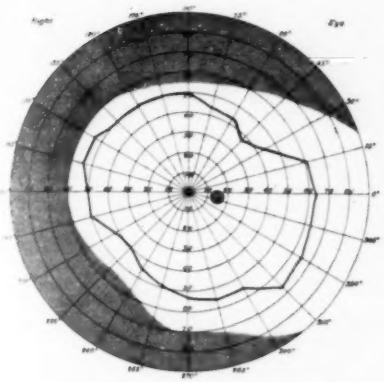

Figure 5

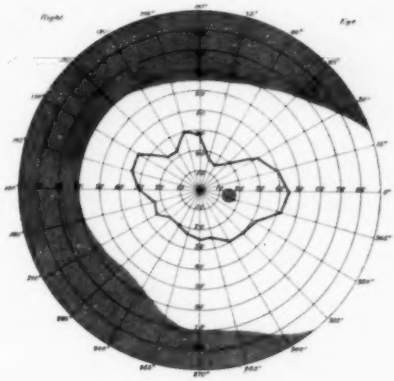

Figure 6

Fig. 5.—Form field taken April 11, 1923, one month after second operation; 5 mm. disk. Vision in the right eye was 20/30 minus; the left eye could not be tested, and the field could not be charted.

Fig. 6.—Form field taken April 27, 1923, three days before third operation; 5 mm. disk. Note marked contraction of field in comparison with Figure 5. Vision in the right eye was 20/40; in the left eye, there was bare light perception. The field could not be charted.

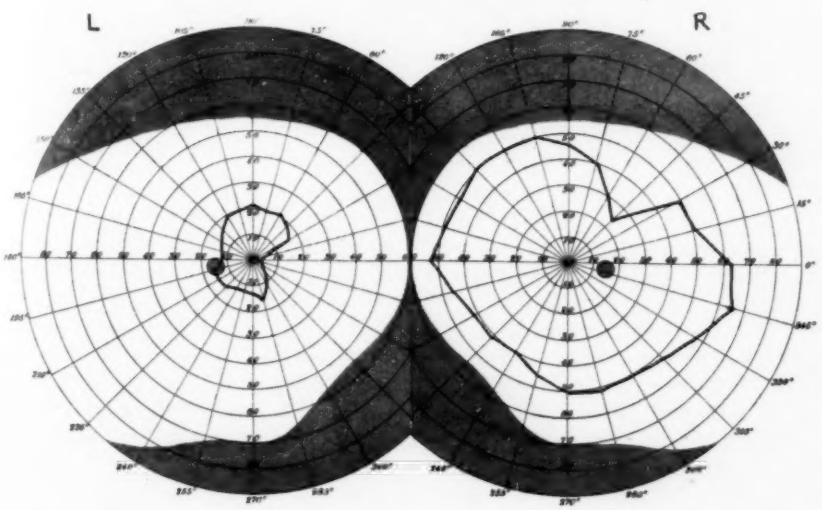

Fig. 7.—Form fields taken July 30, 1923, three months after removal of cyst; 5 mm. disk. Vision in the right eye was 20/30; the left eye could not be tested.

to about 100 F., which lasted for twenty-four hours. During the next five days the temperature remained normal; there was little drainage from the wound, and none into the nose. On the sixth day, the cerebrospinal rhinorrhea recurred, accompanied by a slight chill and a rise of temperature to 101.6 F. A folded gutta percha drain was again placed in the wound. A stormy period ensued for the next two weeks. Drainage of spinal fluid was profuse. The temperature fluctuated from normal to 101.6 F. Part of the time she had rigidity of the neck, a slight Kernig sign and a throbbing headache. It was evident that an extension of the infection had occurred. On May 22, her temperature became normal, although considerable drainage still persisted. On May 26, the drain was shortened and on the 27th drainage ceased. There was no return of rise in temperature, and her general condition was relieved. She

Fig. 8.—Cross section of brain showing cavity of large abscess occupying left temporal lobe caused by secondary infection following removal of infected dermoid cyst. Position and size correspond closely with that of the original dermoid cyst.

was free from headache, and the Kernig sign and stiffness of the neck had disappeared. On June 1, 1923, the drain was permanently removed. During the summer, her general condition was good, and her vision improved materially. Visual fields taken on July 30, 1923, showed decided enlargement of the right field and enough return in the left so that it could be charted (Fig. 7).

In September, she presented symptoms of returning pressure, with headache and choked disk. Paresthesia and motor weakness appeared in the right arm and leg. She became apathetic, and periods of motor aphasia set in. There was an increase of all deep reflexes and diminution of superficial reflexes on the right side. It was only too apparent that a pathologic condition in the left hemisphere was increasing. Was it a return of the cyst or an abscess? The wound bulged and discharged slightly, but no rice bodies were seen. On Sept. 21, 1923, the region of the dermoid cyst was again explored. No trace of the cyst was found, but a mass about the size of a hen's egg was removed from the left

temporal lobe. This proved to be an abscess. Cultures were sterile. Following this procedure, her condition remained critical. The right hemiplegia and motor aphasia persisted until her death on Mach 17, 1924.

Necropsy Findings.—On March 17, 1924, a postmortem examination which was confined to the brain revealed a large abscess in the left temporal lobe (Fig. 8). No trace of the old cyst wall was revealed. Adhesions were present over the base of the brain, vestiges of the meningitis which followed the cyst removal. Sections of the wall of this abscess showed organized granulation tissue which in no way resembled the wall of the original dermoid. The abscess, however, occupied much the same position as the original cyst.

SUMMARY

1. The case presented is that of an intracranial dermoid cyst. The wall resembled true dermis containing hair follicles, sweat glands and stratified squamous epithelium. The central mass was filled with débris composed of desquamated cells, among which were scattered fine hairs and cholesterin crystals. It was attached to the dura in the left temporal region and should probably come under the classification of "meningeal cholesteatoma" suggested by Horrax.

2. The shadow seen in the roentgenograms probably represents a calcified area in the cyst wall, and is almost similar to that reported by Horrax.[14] Such shadows, when seen in cases of suspected brain tumor, should suggest the possibility of a dermoid cyst.

3. The outcome of the case was disappointing. It is not a pleasant task to report one's failures. However, it is not unlikely that the entire cyst wall should have been removed at the first operation, when a permanent cure might have been effected. As it was, the cyst became infected after its first opening, and its ultimate complete removal was followed by local meningitis and brain abscess, from which the patient succumbed.

SIGNIFICANCE OF JACKSONIAN EPILEPSY IN FOCAL DIAGNOSIS OF CEREBRAL LESIONS *

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It is a firmly established fact that morbid processes affecting the motor cortex of the brain may produce convulsions of the muscles of the opposite side of the body. These convulsive seizures are the symptoms of motor irritation. Such localized convulsions are, therefore, referred to as "cortical epilepsy" or jacksonian convulsions. It is generally believed, however, that typical jacksonian seizures do not occur when the subcortical parts of the brain, such as the corona radiata, alone are involved, and that when jacksonian attacks have occurred as the result of cortical irritation, subsequent destruction of the motor cortex or of the subcortical motor pathways will bring about cessation of the convulsions. It was this belief that led Hughlings Jackson to suggest excision of the motor cortex for the cure of certain cases of epilepsy.

Since endotheliomas may originate in the meninges and involve the brain, not by infiltration, but by contiguity and compression of its cortical surface, and since gliomas may originate in the essential cerebral tissues and invade the brain by infiltration of the subcortical regions, the early appearance of jacksonian attacks might serve to assist greatly in determining operability in a given case, since endotheliomas, because of their superficial situation, constitute the form of neoplasm most suitable for removal.

My attention has recently been called to the report of a case by Otto Sittig [1] in Prague in which hemiplegia, aphasia, and choked disk developed gradually. In spite of the fact that at operation an endothelioma measuring 7 by 4.5 by 3 cm. was found, situated on the rolandic convolution, jacksonian convulsions had not occurred. The tumor was removed successfully; some months afterward, however, convulsions occurred, but the character of these seizures was not recorded.

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* From the department of Neurology of the University of Pennsylvania School of Medicine.

* Read by title at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, May, 1924.

1. Sittig, Otto: Med. Klin. **19**:1363 (Oct.) 1923.

In this case the absence of convulsions was remarkable, and for this reason it was reported in detail. Sittig offered the explanation that the slowness in the rate of development of the tumor was a factor, since the cerebral tissues were thus given time for compensation to take place, and that the sudden relief of compression by removal of the tumor was the chief cause for the subsequent development of convulsions.

In attempting to throw light on this subject I have selected the following specimens from the laboratory of neuropathology at the University of Pennsylvania: four cases of cortical tumor; five cases of subcortical gliomas; one case of cerebral softening from thrombosis; one case of pachymeningitis, and one case of acute encephalitis affecting the cortex. I have reviewed and abstracted the histories of these cases, particularly as regards the occurrence of jacksonian epileptic attacks.

CASES OF CORTICAL TUMOR OF THE MOTOR AREA NOT ACCOMPANIED BY JACKSONIAN SEIZURES

CASE 1.—In this case of endothelioma no convulsive attacks were observed, although the motor cortex was compressed sufficiently to cause hemiplegia and aphasia. The tumor was found just above Broca's area, in front of the central fissure. After removal of the tumor the symptoms disappeared

CASE 2.[2]—The patient had a large endotheliomatous tumor of prolonged duration implicating the motor convolution. In this case there was only one bilateral convulsion. No unilateral attacks occurred.

CASE 3.—In this case an endotheliomatous tumor compressed the left motor area. There were three attacks resembling jacksonian convulsions, which began on one side of the face. All limbs, however, were subsequently implicated, the right side being affected more severely than the left.

In each of these cases the convulsions must have been due to cortical irritation, but because of the bilateral nature of the seizures, the focalizing value of the attacks was diminished.

CASE 4.—A tuberculoma destroyed part of the motor cortex and produced hemiplegia, but epileptic attacks were not observed.

CASES OF SUBCORTICAL GLIOMA ACCOMPANIED BY UNILATERAL CLONIC CONVULSIONS

CASE 5.—The patient had frequent attacks of clonic convulsive movements limited to the limbs on the left side. Convulsions did not appear until late in the course of the disease. The tumor, a large glioma, had its origin in the centrum semiovale, and had extended in its growth to a point 2 cm. beneath the right motor cortex.

CASE 6.—The patient had clonic convulsions limited to the facial muscles on one side. The tumor, a very large glioma, originated in the centrum semiovale and extended to a point 3 cm. beneath the motor cortex.

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2. Case 2, was reported by Spiller, W.: Hemicraniosis and Cure of Brain Tumor by Operation, J. A. M. A. **49**:2059 (Dec. 2) 1907.

CASE 7.[3]—The patient developed frequent severe unilateral clonic convulsions. The tumor, although small, was of long standing, the symptoms having been present for eight years. The growth measured 1.5 by 1.5 by 0.5 cm. It was situated in the second frontal convolution and did not extend into the central convolution; it had, however, extended close to, though not quite into the cortex.

CASE 8.—Typical jacksonian attacks occurred, beginning in the arm and forearm, later being limited to the hand. The number and severity of the attacks diminished as the paralysis increased. The tumor—a glioma—reached just to the motor cortex.

CASE 9.—A large subcortical glioma of eighteen months' duration had extended to and finally infiltrated the cortical surface in the lower part of

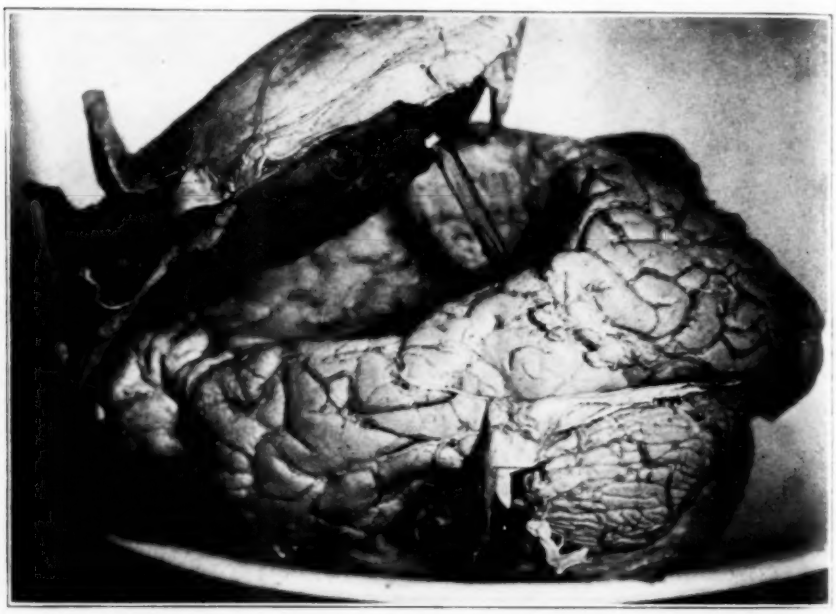

Fig. 1.—Marked compression of the cerebral cortex. Jacksonian convulsions had not occurred.

the motor region and temporal lobe, but no convulsions were recorded. Hemiplegia and aphasia had developed so slowly that the clinical course had resembled that of cerebral thrombosis.

VASCULAR AND INFLAMMATORY LESIONS

CASE 10.—In a case of internal pachymeningitis of one and one-half year's duration, there was a large depression of the cerebral cortex, produced by an extensive hematoma that had caused extreme hemiplegia with spasticity and contracture of the paralyzed limb. No convulsions were recorded.

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3. Case 7 was reported by Spiller in Review of Neurology and Psychiatry, 1907, and in the Transactions of the College of Physicians of Philadelphia for 1907.

CASE 11.—An extensive traumatic, left-sided meningeal hemorrhage of six weeks' duration caused hemiparesis; there were no convulsions. The hemorrhage was terminated by operation. Recovery was complete.

CASE 12.—Thrombotic softening in the anterior part of the right second frontal convolution and thrombotic cyst in the left lenticular nucleus produced paresis of the left side of the body following an apoplectic attack. There was deviation of the eyeballs to the left, with frequent irregular jerking movements to the right. These clonic movements of the eyeballs were suggestive of irritation of the left cortical center of the ocular muscles. No other convulsive seizures occurred.

CASE 13.—The patient had focal encephalitis involving the right precentral gyrus, producing left hemiparesis and repeated convulsions limited to the left hand and left side of the face. (This case was reported by Dr. Mills before the American Neurological Association in Boston in 1906 under the title "Focal Encephalitis.")

COMMENT

In my opinion, in the great majority of instances, a tumor impinging on the central motor cortex will produce jacksonion convulsions at some time during the course of the disease. Exceptional cases may be encountered in which convulsions never develop, or if they do, they are so few as to be inconspicuous features of the disease. The dissimilarity of the effects from apparently analogous lesions in similar situations is difficult to explain.

Cortical irritation due to unilateral lesion may rapidly reach such great intensity as to cause convulsions of the limbs of both sides of the body at the same time, thus greatly diminishing the localizing value of the attack. Associated attacks of aphasia, however, by attracting attention to slight inequalities of the convulsive movements that do occur, and that might otherwise be overlooked when both sides of the body are convulsed at the same time, possess great localizing value.

In order to produce cortical irritation of sufficient intensity to cause jacksonian attacks, it is not necessary for a tumor or other lesion to implicate the motor area directly, for the rolandic convolution can be severely compressed and thus irritated by a lesion situated anterior or posterior to it.

The earlier jacksonian attacks appear during the course of the disease, the greater is their localizing value. When they occur during the late stages and are complicated by increased intracranial tension, they may become less characteristic. In the cases of subcortical glioma recorded here in which jacksonian seizures occurred, the tumors had their origin in the centrum semiovale, and in their growth had extended close to or even into the motor cortex. The proximity of the lesion to the cortex must have been the determining factor in producing jacksonian convulsions as the result of irritation, or else the tension exerted

from within the brain was sufficient to compress the cortical surface against the calvarium, thus indirectly causing irritation.

In each case there was paralysis of the limbs of one side. In two of the cortical and in four of the subcortical tumors, however, convulsions had occurred in limbs already paralyzed, indicating that the motor pathways had not yet been obliterated by the tumor, for the impulses originating in a cortical irritation were still capable of being transmitted to the limbs of the opposite side of the body.

Fig. 2 (Case 7).—Glioma of the cerebral cortex which had caused Jacksonian epilepsy.

It is conceded that a complete section of the motor tract beneath its cortical origin will produce complete hemiplegia on the opposite side, so that under such circumstances the occurrence of clonic convulsions of the paralyzed limbs would seem to be impossible. It is well known, however, that unlike certain other lesions, gliomas do not always destroy uniformly all the axis cylinders embraced within the growth. The partial integrity of the motor tract may explain, therefore, the occurrence

of convulsions in limbs that appear to be completely paralyzed. In Case 8, in which the clonic convulsive seizures diminished in frequency and severity in exact proportion to the rate of increasing paralysis of the affected limb, the tumor—a glioma—had evidently extended so close to the cortex as to destroy the cortical motor cells, thus diminishing their irritability.

Destruction of the motor cortex must inhibit the transmission of impulses. This may explain the absence of convulsions in Case 4—a tuberculoma. On the other hand, it is well known that the frequent repetition of severe clonic unilateral seizures is capable of producing exhaustion of the cortical cells, a condition that in itself is sufficient to cause severe paralysis of temporary nature. The temporary paralysis of exhaustion occurs in cases of idiopathic epilepsy without demonstrable cerebral lesions. A remarkable example of this kind, together with necropsy, was reported by me.[4]

Furthermore, it has frequently been observed that severe hemiplegia may occur when the motor cortex is involved by compression only, and recovery of movement of the limbs may take place when the compressing agent is removed. Extensive lesions of the cortex, such as pachymeningitis or slow dural hemorrhages, may cause hemiplegia and marked compression of the cerebral motor cortex without convulsions. Since this form of compression develops slowly—in Case 10 many weeks were required for the production of symptoms—it thus appears that the cortical brain cells are capable of adjusting themselves to new conditions and may become less susceptible to irritation provided the onset and the course are slow. In more rapidly developing vascular lesions, however, such as certain inflammatory conditions, as in Case 13, and in some cases of thrombotic softenings, there is no time for compensation to take place, and violent unilateral seizures may occur.

In certain cases gliomas may grow very slowly, as, for example, in Case 9, in which, at times, there were attacks resembling apoplectic seizures, with gradually developing hemiplegia. Convulsions may not occur, and yet the growth may actually infiltrate the cortical surface of the brain. In these cases the symptoms may be confused with those of thrombosis of the sylvian artery. Bickel and Frommel [5] reported six cases of this kind in which the symptoms resembled those of progressive thrombosis, being insidious in onset, with successive mild apoplectiform attacks, but no symptoms of intracranial pressure. These

4. Cadwalader, W. B.: Idiopathic Epilepsy Complicated by Motor Aphasia and Diplegia, with Necropsy, J. A. M. A. **51**:1778 (Nov. 21) 1908.

5. Bickel, G., and Frommel, E.: Rev. méd. de la Suisse Romande, Geneva **44**:33 and 45 (Jan.) 1924.

investigators found that the tumors were gliomas, and that they were always situated in the deeper regions of the centrum semiovale. They referred to thirty cases of multiple foci of encephalomalacia—one presented a clinical picture that was the reverse of that just described. As the symptoms pointed to brain tumor, even choked disk and apoplectiform seizures having been present, a presumptive diagnosis of subcortical tumor of the right hemisphere had been made, but necropsy revealed the presence of multiple foci of encephalomalacia.

PORENCEPHALY *

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Porencephaly was first described under this name by Heschl,[1] who, in 1859 and subsequently, gave a detailed description of eight cases. According to Audry,[2] the defects described by Reil in 1912 were porencephalic.

Kundrat,[3] in 1882, studied twelve such brains and added to his report an analysis of all previous publications. In 1889, Schattenberg [4] published a detailed summary of the records of thirty-two other cases recorded by various authors. A review by von Kahlden,[5] in 1895, included ninety-four cases and a clear microscopic and macroscopic description of ten, coming under his own observation. The analysis by Schutte,[6] in 1902, of 123 cases is mainly devoted to the gross alterations. Another good discussion is that by Salzmann.[7] In general, the references to the literature in each of the contributions mentioned are thorough, and there have been but few recent reports. Most of the studies have been devoted to the gross anatomic alterations.

By different authors the definition of porencephaly varies in some small particulars. It is, however, accepted that the condition is a defect communicating with the ventricles or separated from them by a thin layer of brain tissue, and covered on the outside by the arachnoid. The location, according to Von Kahlden,[5] in the lower portion of one or both central and the dorsal parts of the adjoining frontal gyri, is characteristic. He believes that the name porencephaly should be applied only to such defects as are acquired during intra-uterine life and not

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*From the Pathology Laboratory of Rush Medical College.

1. Heschl, R.: Gehirndefect und Hydrocephalus, Prag. Vrtljschr. f. d. prakt. Heilk. **61**:59, 1859; Ein neuer Fall von Porencephalie, ibid. **72**:104, 1861; Neue Fälle von Porencephalie, ibid. **100**:40, 1868.

2. Audry: Les porencéphalies, Rev. de méd. **8**:462, 1888.

3. Kundrat, H.: Die Porencephalie, Eine anatomische Studie, Graz, Leuschner & Lubenski, 1882.

4. Schattenberg, R.: Ueber einen umfangreichen porencephalischen Defect des Gehirns bei einem Erwachsenen, Beitr. zur allgem. Path. u. path. Anat. **5**:119, 1889.

5. Von Kahlden, C.: Ueber porencephalie, Beitr. zur path. Anat. u. Allgem. Path., **18**:231, 1895.

6. Schutte, E.: Die pathologische Anatomie der Porencephalie, Zentralbl. f. allg. Path. u. path. Anat. **13**:633, 1902.

7. Salzmann: Zur Kentniss der porencephalie im frühen Kindesalter, Inaug. Dissert., München, 1913.

due to trauma. Siegmund,[8] however, combined under the name porencephaly all defects due to destruction unaccompanied by infection. In his opinion, all are acquired, and he does not favor the classification of congenital and acquired porencephalus. Bourneville and Schwartz[9] differentiate between a true and false porencephaly, the former induced by disease of intra-uterine or extra-uterine life, the latter by disturbances of circulation. Any porus in the brain which does not communicate with the ventricle is called pseudo-porencephaly by Obersteiner.[10] Kundrat,[3] on the other hand, applies the name to any defect roofed over by the arachnoid.

Various causes of porencephaly have been described. Schutte,[6] for example, mentions diseases of the brain in the fetus, inflammatory processes during intra-uterine or extra-uterine life, embolism and thrombosis, primary internal hydrocephalus, primary disturbances of development with secondary hydrocephalus, and intra-uterine (intrapartitum) or extra-uterine trauma. Disturbances of nutrition in the mother, anomalies of placental development and cramplike contractions of the uterus are assumed by Kundrat to bring about ischemic necrosis, and this in its turn, porencephaly by resorbtion. He believes the circulatory disturbance is in the deeper arterioles of the white matter, with a later involvement of the cortex. These views are accepted by many other investigators. On the other hand, some, like von Kahlden and Schattenberg, attribute it to disturbances of fetal development, a defect of the anlagen, a view only partially accepted by Siegmund, who ascribed the defects to necrosis, the origin of which greatly varies, all the way from circulatory disturbances to birth trauma.

The location is not always as stated. Holtby[11] reported a bilateral porencephaly in a woman, 73 years old. Siegmund[12] reports that in 122 cases of porencephaly, the region of the central fissure was most frequently affected. The frontal lobes were involved in seventeen, the temporal lobes in thirteen, the occipital in fourteen and the basal ganglions in twenty-four.

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8. Siegmund, H.: Die Entstehung von Porencephalien und Sklerosen, Virchow's Arch. f. path. Anat. u. Physiol. **241**:237, 1923.

9. Bourneville and Schwartz: Nouvelle contribution à l'étude de la pseudo-porencéphalie et de la porencéphalie vraie, Progrès méd. **8**:9-37, 1898.

10. Obersteiner, H.: Anleitung beim Studium des Baues der nervösen Zentralorgane im gesunden und kranken Zustande, Leipzig and Vienna, 1812, p. 68.

11. Holtby: A study of Porencephaly with Special Reference to a Case of Symmetrical Lesion Affecting the Temporal Poles of the Cerebrum, Tr. Royal Acad. Ireland **36**:207, 1918 and 1920.

12. Siegmund, H., cited by Holtby.

The diagnosis and prognosis depend on the site and extent of the lesion. Where there is deep-seated destruction of the nervous elements, involving vital parts or important communication centers, there will be signs of spasticity and severe motor disturbances with or without mental symptoms. In such cases, death generally occurs within a few weeks or months. If, however, the defect is superficial, there may be few or no symptoms, and the presence of the lesion is detected only at necropsy. That porencephaly is not necessarily fatal in early life is indicated by the following table by Schattenberg:

Deaths from Porencephaly According to Age

Period	Number of deaths
0 to 1 year	12
1 to 10 year	11
10 to 20 year	14
20 to 30 year	3
40 to 50 year	4
50 to 60 year	2

Frequently necropsy is not performed, and therefore the frequency may be greater among those living to an old age than the table indicates.

The following are accounts of four porencephalic defects studied by us—two in adult and two in infant brains. The brains were hardened in 10 per cent. formalin, and pieces for microscopic examination taken from the cortex adjoining the porus, the frontal, temporal and parietal lobes away from the porus, the corona radiata, the right and left lenticular nuclei, the caudate nuclei with the internal capsule, the thalamus, the substantia nigra and nucleus ruber, the isthmus, the cornu ammonis, the pons, medulla, cervical region of the spinal cord and the dentate nucleus of the cerebellum with the surrounding cerebellar arborizations. The following stains were used: hematoxylin and eosin, phosphotungstic-acid-hematoxylin, Heidenhain's iron hematoxylin, toluidin blue, van Gieson's and Mann's stains; Ciaccio's and Sudan III, for fat; also Bailey's [13] stain for fibrillary neuroglia.

REPORT OF CASES

Case 1.—*History.*—A negro laborer, about 45 years old, was brought to the hospital of the house of correction from an incoming train, where he was found with frozen feet. He entered semistuporous, and answered questions with difficulty. His reflexes were normal, and there was no alcoholic odor to his breath. Eleven days after admission, he died. No diagnosis of any alteration of the central nervous system was made.

13. Bailey, P.: A New Principle Applied to the Staining of the Fibrillary Neuroglia, J. M. Res. **23**:73, 1923.

Anatomic Diagnosis (E. R. LeCount).—This diagnosis was made: Porencephalus; marked hyperemia of the brain and the leptomeninges; foramen magnum furrow of the cerebellum; multiple confluent petechial hemorrhages into the lining of the duodenum and urinary bladder; slight hypostatic hyperemia and edema of the lungs; passive hyperemia of the liver and kidneys; lessened yellow material of the suprarenal cortices; fatty changes of the liver, aorta and coronary arteries; marked hypertrophy of the heart (left ventricle); caseous nodular tuberculosis of the liver; localized fibrous pleuritis; pigmented scars of the legs. The hardened brain weighed 1294 gm. The cerebral convolutions were flat, and all the sulci were almost obliterated. The cerebral veins were flat and mostly empty, and the finer arterioles of the leptomeninges were invisible. The leptomeninges were transparent. In the right frontal lobe and adjoining the tip of the temporal lobe, there was a protruding, soft gelatinous mass, 7.3 by 5 cm., with an uneven surface and somewhat lobulated. It involved completely the posterior two thirds of the inferior frontal and the greater portion of the medial frontal gyri, and was sharply bounded below by the temporal lobe, which was not

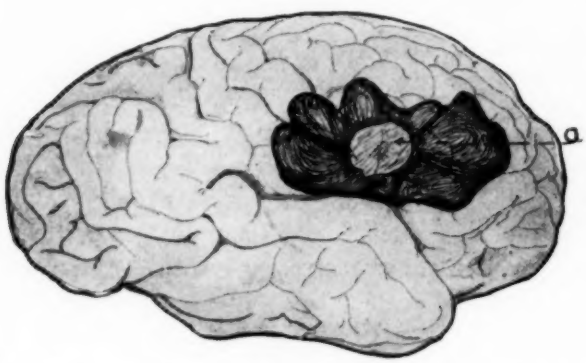

Fig. 1 (Case 1).—Cystic mass with cartilaginous thickening (*a*) in the arachnoid and overlying the center of the porencephalus.

involved from the outside. Over its center, there was a cartilage-like plaque about 12 by 14 mm. (Fig. 1). In segments of the brain, the porus extended 7.5 cm. from the front backward, and measured 6 by 3.7 cm. in its largest lateral dimension. It did not communicate with the ventricle, but was separated from it by a thin band 3 to 5 mm. thick (Fig. 2). The structures replaced by it were the medial and inferior frontal gyri and almost the entire head and part of the body of the caudate nucleus. The right ventricle was compressed to a narrow slit, the left wider than normal. The corpus callosum was narrow, the cerebral fissures closely compressed. The right hypocampal gyrus was raised and projected at the base of the brain stem on that side. The cerebral arteries were empty, their walls slightly thickened. There was no stippling of surfaces made by cutting. In its frontal half the brain was asymmetrical, the right hemisphere 6 and the left 4 cm. from the lateral ventricle to the periphery of the brain at the level of the anterior commissure. In the upper fiber tract of the pons, there were two distended veins almost continuous with each other, 7 by 2 mm. and extending 8 mm. from the front backward. There were no other gross changes.

Histology.—The porus was filled with a homogeneous, pinkish substance in which there were cavities resembling perivascular lymph spaces. There was no visible membrane, and in some places, the extremely vacuolated tissue appeared like a continuation of the cyst. Near the cyst the pyramidal cells of the cortex were hydropic and pale, but further away unchanged. The right lenticular nucleus was extremely fenestrated; the vessels were all empty, and there were large empty spaces surrounded by fenestrated brain tissue containing dense masses of "hyaline bodies." The nerve cells stained poorly. Their nuclei were swollen and excentric, and in many instances only a shadow of a cell body could be seen. The cornu ammonis was extremely edematous, and the perivascular lymph spaces were considerably larger than normal. In sections of the motor cortex, corona radiata, left corpus striatum, thalamus, substantia nigra, nucleus

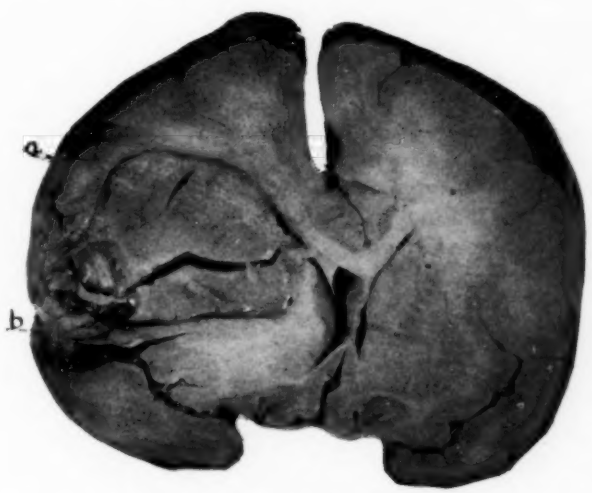

Fig. 2 (Case 1).—Caudad surface made by a coronal section through the third ventricle; *a* and *b* indicate the upper and lower limits of the fluid coagulated by formalin in the porencephalic cavity.

ruber, medulla, pons, cervical portion of the spinal cord and dentate nucleus of the cerebellum with its cortical arborizations, there was marked edema. The veins were mostly empty—a few distended with blood. Many of the smaller arterioles had calcified walls, and in the meshes of the leptomeninges at the base of the brain were a few endothelial and plasma cells. There was no hemorrhage or blood pigment present. The Nissl granules in some of the large ganglion cells of the internal capsule and also of the Purkinje cells in the cerebellum varied greatly in distinctness. In many, they were crowded about the nucleus; in others, at the periphery of the cell; in some they were almost invisible. In the majority of the cells there were no changes, except those usually found with edema.

In this case, the cerebral convolutions were well developed, and therefore the porus had evidently been acquired late in life. We assume that it was due to ischemic necrosis with subsequent cyst formation (oedema ex vacuo).

Case 2.—*History.*—M. P., German, 62 years old, a stable man, single, was brought to Cook County Hospital (service of Dr. Cubbins), with a diagnosis of suspected skull fracture on Jan. 24, 1922. He had fallen down stairs, striking his head. He was first placed in a blanket in an oat bin, and later on a cot in the barn. Being dazed and unable to talk, it was thought he was drunk. For two days, he did not eat or drink, slept most of the time, and would not answer questions, cursing and struggling when interfered with. His employer called a physician, who sent him to the hospital. He had a rectal temperature of 99.4 F. on entrance, a pulse rate of 90, and the respirations were 24. There was no external injury of the head, and no bleeding from the nose or ears. There was a little purple discoloration of the eyelids, some tenderness and rigidity of the neck, and stiffness of the extremities, but no paralysis. The cerebrospinal fluid was turbid and bloody. He remained irrational, and gradually grew worse. On January 30, occasional râles were heard in the chest, and his temperature went up to 102.4 F. (rectal). He died soon afterward.

Anatomic Diagnosis (E. R. LeCount).—The diagnosis was: Extensive comminuted fracture of the cranium; bruised and torn brain; extensive traumatic hemorrhage into the deep scalp tissues and deep tissues of the face and neck; old injury of the brain; early hypostatic bronchopneumonia; acute emaciation; localized fibrous bilateral pleuritis; atrophic pulmonary emphysema; slight senile sclerosis of the aorta; absent left testicle. The brain after hardening in formalin was symmetrical, the cerebral convolutions flat, the sulci entirely obliterated. The cerebral veins were engorged and their finer radicles prominent. The pia-arachnoid was transparent, except where there were dark brown clots along the vessels of the vertex of the brain, but especially over the right parietal lobe. The medial one fourth of the right precentral and postcentral gyrus was extremely narrow, thus forming a pit or depression about 3 cm. in diameter, this microgyrus being overlapped by the lobulus parietalis superior. The narrowing of the gyri was especially evident in segments made by coronal sections and when the two sides were compared. At the base of the right temporal lobe, the cortex was bruised and lacerated. About 5 cm. cephalad from the tip of the right occipital lobe, there was an old defect on the mesial surface extending laterally into the right inferior horn. Its largest transverse diameter was 3.4 cm., and it was 4 cm. deep. A thickened dura consisting of many folds of the falx cerebri was carried into the cavity and adhered tightly to its walls, which in the anterior half was covered with a closely adherent pia-arachnoid.

In coronal sections at the level of the third ventricle, the white matter of the corona radiata was missing, and the undermined convolutions of the cortex were exposed (Fig. 3). The right inferior horn at that level was very wide, the cornu ammonis almost completely obliterated. At the level of the anterior commissure in the longitudinal sulcus, there was a defect about 1.5 cm. in diameter involving slightly the cortex of the left hemisphere but communicating in the right hemisphere with the lateral ventricle. The left lateral ventricle was compressed to a narrow slit about 1 mm. wide. Surfaces of segments were markedly stippled. The gray matter of the cortex throughout was narrower than normal. There was complete absence of the corpus callosum and the gyri cinguli were directly in contact with the corpus striatum and thalamus on both sides (Fig. 9). The cerebellum was compressed from above downward, and there was a shallow groove at its base corresponding to the edge of the foramen magnum. The arteries at the base of the brain were slightly thickened. There was no other gross change.

Anatomic Diagnosis.—The diagnosis was: Old acquired porencephalus in the right cerebral hemisphere; agenetic absence of the corpus callosum; old, focal, traumatic pachymeningitis; recent traumatic hemorrhage into the leptomeninges and laceration of the brain cortex; marked unilateral internal hydrocephalus; marked general atrophy of the cerebral cortex; focal microgyria; edema and hyperemia of the leptomeninges; slight sclerosis of the cerebral arteries.

Histologic Examination.—In sections of the precentral, postcentral and parietal cortex, the centrum semiovale, caudate and lenticular nuclei with the internal capsule, thalamus, cornu ammonis, pons, medulla, spinal cord and cerebellum, there was more or less vacuolization, according to the distance of the tissue from the porus and trauma. Some of the veins were empty and collapsed. The arteries were somewhat sclerosed, and some of the small arterioles in the corpus striatum and thalamus were calcified. Sections from the superior and medial frontal cortex and gyrus cinguli adjoining the porus

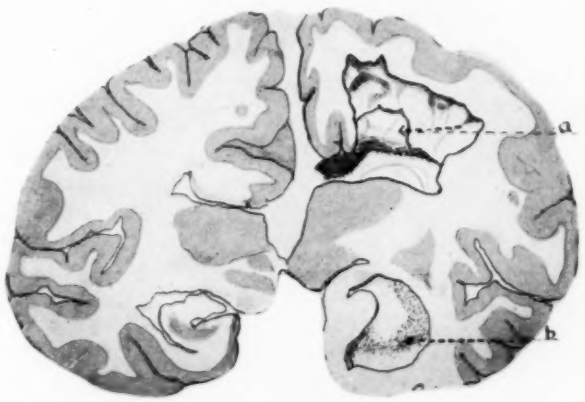

Fig. 3 (Case 2).—Drawing, natural size (over glass plate), of ventral surface made by a coronal section just behind the splenium of the corpus callosum. Here the porus has its outer opening on a mesial surface; (*a*) indicates a porus; (*b*) distended inferior horn.

were fenestrated and contained small hemorrhages. Small fresh hemorrhages were also in the adjacent white matter, and in the leptomeninges of the gyri mentioned. The pyramidal and ganglion cells in these regions were swollen and pale, and had excentric and poorly-staining nuclei and only a shadow of cell body. The large ganglion cells in the medulla, pons, spinal cord and cerebellum were somewhat hydropic but otherwise unchanged, with the Nissl granules very distinct. The ependymal lining of the lateral ventricles near the porus had nodular projections from 0.1 to 1 mm., but away from the porus it was normal. The subependymal layer, however, was extremely vacuolated and fenestrated, and the nerve cells in this region were swollen, with hardly visible nuclei and faintly staining cell bodies. The ependymal vessels were all empty and shrunken.

Histologic Diagnosis.—Recent multiple traumatic hemorrhages in the brain cortex and leptomeninges; nodular hyperplasia of the ependyma; slight sclerosis and focal calcification of the cerebral arteries; edema, disseminated hyperemia and anemia of the brain were diagnosed.

This porus was combined with recent traumatic brain lesions and an agenesis of the corpus callosum. The site of the porencephalic defect is rather unusual, and the folds of the dura in the cavity speak very strongly for trauma as the cause.

Complete or partial absence of the corpus callosum in connection with porencephaly is not rare, and has been described by many authors as a defect per se. There are no characteristic symptoms. From a list of sixty-one reports collected and analyzed by Bianchi,[14] thirteen patients were of normal mentality, twenty abnormal, and in fifty-eight the character could not be ascertained.

Case 3.—*History.*—An illegitimate child, about 1 year old, was brought to the Presbyterian Hospital, Oct. 1, 1920. The mother said it had been large and fat until six months before, when she had put it out to board, and then it had lost weight. It was in the Children's Memorial Hospital for three days, and was discharged with the statement that it should be placed in a private boarding place, as it only needed food. It was an emaciated infant weighing 10 pounds, 9 ounces (4.8 kg.), with a large head, the fontanelles open, marked rigidity of the extremities, the fingers clenched and the feet in carpopedal spasm. The knees and hips bent with difficulty. The neck muscles were flaccid, the heart beat was rapid and somewhat fetal in character. The chest flared out with hyperplasia of the ribs and cartilages at their junction. The abdomen was soft, protuberant and flaccid, and the buttocks were wrinkled, the prepuce adherent, the left testicle high but movable, the knees and wrists rather large, and in and behind the left submaxillary region there was a firm swelling. This later developed into an abscess that broke and discharged a sanguinolent fluid and pus; nystagmus was present. On October 9 there were: hemoglobin, 80 per cent. (Tallquist); white count, 16,400; red count, 5,150,000; pulse rate, 108; temperature, 99 to 102 F.; respiration, 36 per minute; Wassermann test, negative.

There was not much change in the baby's condition during its stay at the hospital, except that marked opisthotonos also developed. On October 31, the baby died.

Anatomic Diagnosis (Dr. Raulston).—Porencephaly, emaciation and anemia, hyperemia of the mucosa of the colon, small patent foramen ovale and small open anterior fontanelle were noted. The hardened brain weighed 528 gm. It was asymmetrical, the left hemisphere somewhat wider than the right. The cerebral convolutions were well rounded but irregular in their arrangement, and the cortical landmarks in the frontal lobe were made out with difficulty. At the site of the operculum on each side, the gyri radiated more or less centrally toward holes, 2 cm. by 1.5 cm. and 3 cm. by 1.5 cm., left and right, respectively (Fig. 4), over which the leptomeninges were slightly turbid. Elsewhere the leptomeninges were somewhat raised by fluid, but otherwise they were clear and transparent. The cerebral veins were almost empty, and their finer radicles invisible. The arteries at the base of the brain were thin-walled and normal, grossly. In coronal segments, the pit on the left side communicated by a small opening with the lateral ventricle. On the right, it was separated by a narrow bridge of white substance about 2 mm. wide. The gyri surrounding the defects were

14. Bianchi, A.: Studio anatomica di un cervello senza corpo calloso, Arch. ital. di anat. di embriol. **3**:688, 1924.

narrow and asymmetrical, especially those forming the opercula. The ventricles were greatly distended and encroached on a large portion of the white substance. The foramina of Monro formed a semicircular canal widely open into the lateral ventricles. The corpus callosum was narrow and at the splenium formed exclusively by the ependymal lining. The inferior and posterior horns were very much enlarged. The septum pellucidum was thin and in many places perforated. The central nuclei were compressed but otherwise unchanged. A white strand about 1 mm. in diameter crossed the left ventricle and was attached on each end to the ependyma (Fig. 5). There was no other gross change. The diagnosis was: Moderate bilateral porencephalus and microgyria; marked internal hydrocephalus; edema and anemia of the brain and the leptomeninges.

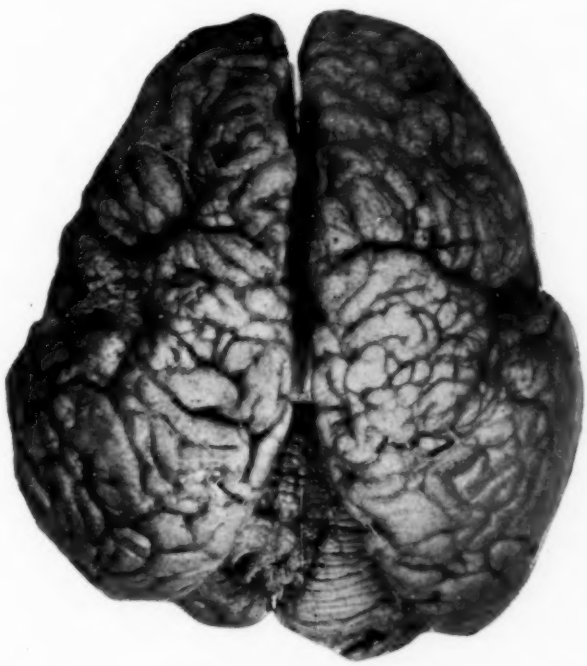

Fig. 4 (Case 3).—Bilateral symmetrical porencephalus where the frontal and temporal lobes join, with marked microgyria about the defects.

Histology.—Sections of the right and left superior, medial and inferior frontal gyri; the right and left cornu ammonis, the brain stem, pons, cerebellum and various sections of the medulla and spinal cord were edematous. There was extensive vacuolization especially in the cortex about the porus, with the small pyramidal cells surrounded by large spaces, pronounced because these cells were considerably shrunken compared with the large ganglion cells in the floor of the brain stem and in the medulla. The latter were hydropic and swollen, with an irregular, indented cell body. The pia-arachnoid was raised, the fibrils were pushed apart, and there was general evidence of a marked edema. Some of the cerebral and leptomeningeal veins and capillaries were engorged; all the arteries were more or less empty. In the leptomeninges of the superior frontal gyrus,

there was a scar about 1 by 1.5 mm. in diameter consisting of fibroblasts, fibrils, endothelial cells and glia cells, but there was no evidence of any other inflammatory process.

Histologic Diagnosis.—The diagnosis was: Marked edema and hyperemia of the brain and the leptomeninges; atrophy of the pyramidal cells and hydrops of the large ganglion cells.

In this third case, the lesion was bilateral, and there was marked microgyria in the neighborhood of each porus, with stellate radiations of the corresponding convolutions. This radiation is considered by Kundrat as typical of congenital porencephalus, but it was also found by von Monakow [15] in two cases of trauma after forceps extraction. The presence of microgyria in porencephaly has been recorded by various

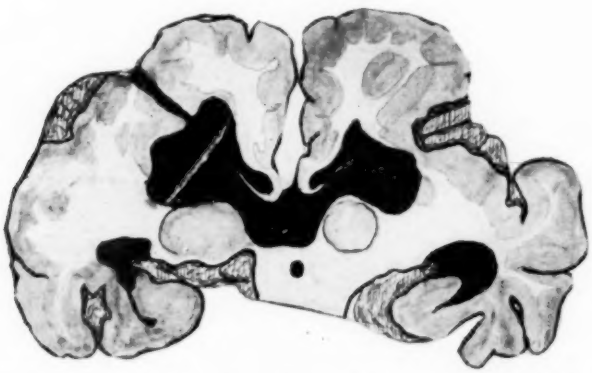

Fig. 5 (Case 3).—Ventral surface obtained by a section through the inferior horns. On the right side there is no communication with the lateral ventricle.

authors, the site of predilection generally being near the porus, but occasionally involving other portions of the brain cortex (Kotschetkova [16]). The general aspect of this brain with its deep sulci and furrowed gyri, associated with the marked anemia and edema, the symmetry of the porus and the microgyria suggest a congenital disturbance of development due to lack of a normal blood supply. Internal hydrocephalus is of frequent occurrence in porencephaly either unilateral or bilateral, and the septum pellucidum has been found defective or completely missing in many instances.

Case 4.—*History.*—On Aug. 1, 1920, a colored baby girl was brought to St. Luke's Hospital. The mother had been ill since its birth two weeks before. The child did not nurse well, and had three convulsions on the day of admission. It was emaciated, listless, with retracted head. There were no gonococci in

15. Von Monakow, C., cited by Siegmund, Footnote 8.

16. Kotschetkova: Beitr. z. path. Anat. der Microgyria und Microcephalie, Arch. f. Pschiat. **34**:39, 1901.

material from the vagina. The mother had been delivered by a midwife and had been sick since the birth, but the nature of the illness was not ascertained; there were no other children. The child weighed about 6.5 pounds (3 kg.), had an apathetic facial expression, retraction of the head to the right with no evidence of fracture, absence of pain on flexing the head, flat chest, dry umbilical cord, and a rectal temperature of 96.6 F. It was put on mother's milk (cow's milk when the other was not obtainable) and although regurgitating much, was fed thus until September 2, when catheter feeding was begun. The child lost weight steadily, and was comatose during the entire period, with the head in extension. A Wassermann test and cell count of the spinal fluid were negative. On November 20, the child weighed 5 pounds, 13 ounces (2.7 kg.) and the feeding formula was changed. On November 24, there was profuse conjunctival discharge, and Dr. Brawley found a left corneal ulcer, with beginning

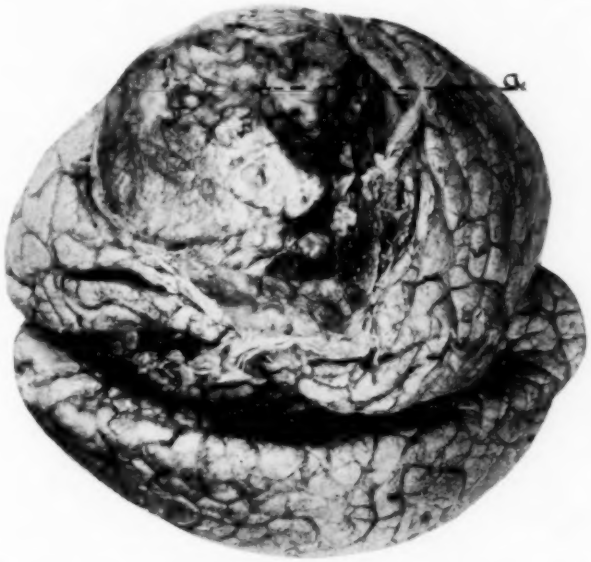

Fig. 6 (Case 4).—Huge porus involving almost one half of the right cerebral hemisphere with nodular hyperplasia (*a*) of the ependyma.

panophthalmitis the following day. On December 9, a bedsore developed on one buttock.

On Jan. 7, 1921, the baby weighed 7 pounds, 3 ounces (3.45 kg.). The food formula was again changed and cod liver oil increased. The weight steadily rose to 10 pounds, 7 ounces (4.6 kg.). On February 21, the temperature began rising and went up steadily to 108 F. per rectum. The blood count on March 9 was 17,800 white cells, and a diagnosis of bronchopneumonia was made. On March 30, the child was very spastic, food being regurgitated; the stools were small, round and formed at first, and later liquid. Accordingly food was discontinued and water only was given. Respiration became very rapid, irregular and finally ceased. In the urine, March 29, many gram-positive diplococci, gram-negative bacilli and leukocytes were found, together with a trace of albumin. There were no organisms in the conjunctival exudate. A Wassermann test of the blood was negative.

Anatomic Diagnosis (J. A. Bargen).—The diagnosis was: Marked right porencephalus; slight prominence of the right eyeball; markedly patent anterior fontanelle; marked hydronephrosis and hydro-ureters with obstruction to their entrance into the bladder; marked fusiform dilatation of the eosphagus; generalized emaciation and anemia; marked hypostatic hyperemia of the lungs; clot-distended right heart chambers; marked fatty changes of the liver; slight

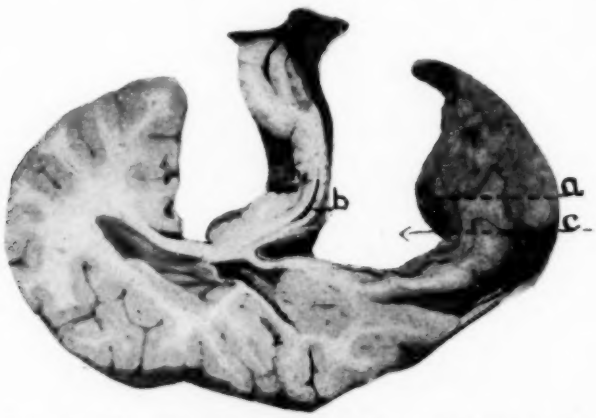

Fig. 7 (Case 4).—Ventral surface obtained by a section through the head of the caudate nucleus; *a* indicates the hyperplastic ependymal lining; *b*, splitting of the corpus callosum; *c*, porus opening widely into the right lateral ventricle.

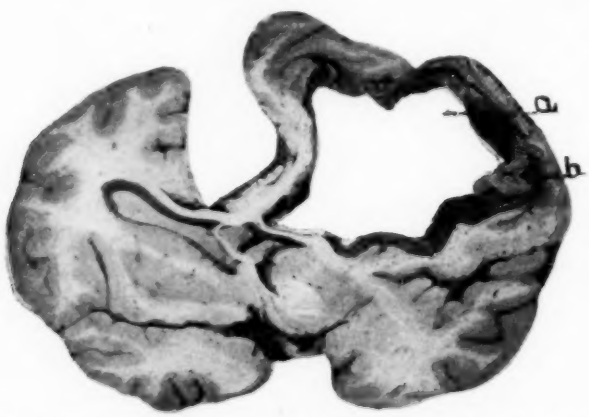

Fig. 8 (Case 4).—Ventral surface obtained by a section at the front margin of the optic chiasma; *a* indicates porus with its outer opening not evident in this segment; *b*, nodular hyperplasia.

fatty changes of the kidneys; slight acute serofibrinous pericarditis and peritonitis.

There was no injury of the deep scalp tissues, but there was marked protuberance of the upper angle of the right occipital bone. All the suture lines were closed except at the anterior fontanelle. The calvarium was removed with difficulty because of adherence to the top half of the dura and the thinness of the bones. It weighed only 70 gm. The cerebrospinal fluid was clear.

The hardened brain (Fig. 6) was asymmetrical, the right frontal lobe 12 mm. wider than the left at the level of the anterior commissure. The cerebral veins were filled with blood, but the finer ramifications of the arteries were hardly seen. The pia-arachnoid was transparent and thin and could be easily peeled from the greater portion of the brain. In the right frontal lobe, there was a cavity 8.5 cm. long, 8 cm. wide and 6 cm. deep, in direct communication with the right lateral ventricle. The white matter of the corona radiata here was absent, and of the superior and medial frontal gyri there was only a narrow band left forming the roof of the cavity in the posterior one third of the frontal lobe. In its anterior portion, the roof was formed by the pia-arachnoid. The floor of the cavity was formed medially by the fornix (Fig. 7) and laterally by the inferior frontal gyrus. The medial wall of the cavity consisted mostly of a thickened ependyma and cortical remains of the gyrus cinguli. The corpus callosum was separated lengthwise and partially in two layers (Fig. 8). The ependymal lining of the porus was covered with numerous firm, gray wartlike elevations from 2 to 5 mm. in diameter (Fig. 9). In places they were confluent and projected from almost the whole remaining tissue of the frontolateral part

Fig. 9 (Case 4).—Side view of the hyperplastic ependyma with wartlike projections.

of the right hemisphere, which was closely welded with the ependymal lining and sharply differentiated from the adjoining brain tissue below (Fig. 8). This tissue was considerably harder than the rest of the brain substance, and contained pale greenish-yellow cysts 5 to 10 mm. in diameter. The ependyma was loosened from the medial and inferior portion of the ventricular wall, normally in place only laterally at the site of the nodular hyperplasia, and was closely connected with the firm tissue. The porus involved the white matter and the cortex exclusively, and the central nuclei were (grossly) unchanged. The left lateral ventricle was also enlarged, 3 cm. wide at the level of the anterior commissure and with the anterior and posterior horns correspondingly increased in size far into the frontal and occipital lobes. The third ventricle was a cavity 1.5 cm. in all dimensions. The gray matter of the cortex and central nuclei was well differentiated from the white substance of the brain, and the vascular dots and striations were rather more pronounced than normal. The arteries at the base of the brain were narrow and empty but otherwise normal, and there was no change in the rest of the large cerebral arteries exposed by coronal sections. The left half of the pons was smaller, and the right half was somewhat larger than normal. The cerebellum was unchanged.

Anatomic Diagnosis.—The diagnosis was: Marked unilateral porencephalus; marked internal hydrocephalus; nodular hyperplasia of the ventricular ependyma;

unilateral atrophy of the pons; edema and hyperemia of the brain and leptomeninges.

Histology.—The hyperplastic papillary growth in the ventricular ependyma had a heterogeneous appearance. From the ependymal lining there were dense masses of ependymal cells extending toward the periphery, where they became mixed with glia cells of several types—large oval glia with pale-staining nuclei, of irregular shape, with here and there a cell with two or three nuclei. In places, the tissue was very vascular, and the glia cells were numerous. They formed dense masses or small foci with radial arrangement (Fig. 10). There were multiple engorged veins and arterioles, many of the latter calcified, and some

Fig. 10 (Case 4).—The hyperplastic ependyma with dense focal overgrowths of neuroglia cells; in the lower part of the illustration, glial nests in aster formation.

appeared as if the vessel wall had been dusted with finely granular lime deposits. Some arterioles were a dense black mass surrounded by a large perivascular space. There were some large foci of hemorrhage, the center of which still showed the remains of a torn vessel surrounded by calcium granules varying in size and shape. The adventitia and adventitial space of some arteries were filled with plasma cells and glia cells filled with minute fat globules (Körnchenzellen) and these were in clusters or more sparsely disseminated in the wide-meshed and fenestrated tissue of the necrotic foci. Multilocular cysts, 2 to 12 mm. in diameter, filled with a material which stained homogeneously, were present. The cerebral cortex adjoining the porencephalic cavity was entirely devoid of normal pyramidal cells; there were many glia cells. The pia-mater was wide-

meshed, containing many plasma cells, and lymphocytes and in some regions had a massive infiltration with glia cells. The large ganglion cells were smaller and fewer in the smaller half of the pons, and the tissue was more fenestrated. In the cervical portion of the spinal cord, there was moderate hyperemia and edema throughout, with no noticeable difference between the anterior horn cells of the right and left sides. The cerebellum was edematous and hyperemic; the ganglion cells of the dentate nuclei and the Purkinje cells were atrophic.

In all other sections of the brain, the tissue was greatly vacuolated and for the most part hyperemic. The arteries were thick and fibrous, and near the porus some in lengthwise sections appeared as solid fibrous strands with very little or no muscle fibers. In the thickened adventitia of several arteries and veins of both the brain and leptomeninges, there was a moderate lymphocytic infiltration. This was most pronounced adjacent to the porus where it was dense. There was a similar exudate in the leptomeninges at the base of the brain, but in a much less degree. The ependymal lining in the left third and fourth ventricles and aqueduct of Sylvius was extremely edematous, and most of its cells were more or less atrophic. There was a uniform and general decrease of nerve cells throughout and an increase of glia cells and glia fibrils in all the sections. The Nissl granules were seen faintly in the pyramidal cells of the cortex and the large ganglion cells, especially those in the floor of the fourth ventricle and aqueduct of Sylvius.

Histologic Diagnosis.—The diagnosis was: Moderate disseminated chronic meningo-encephalitis; sclerosis of the cerebral arteries; focal calcification of the arteries in the brain cortex; marked edema and hyperemia of the brain; marked internal hydrocephalus; nodular hyperplasia of the ependymal and glia cells.

The inflammatory changes in this brain and its leptomeninges characterized by adventitial and perivascular infiltration of lymphocytes were described by Strümpell,[17] von Limbeck,[18] and more recently by Globus [19] and by Winterode and Lewis.[20] The enormous porus in this instance must have had its origin during the latter half of intra-uterine life, and there was possibly a relationship between the child's defect and the mother's illness. We are inclined to believe that the meningo-encephalitis here was of syphilitic origin, even though the spinal Wassermann test was negative. The sclerosis of the arteries supports this view. An unusual feature in this brain was the marked hyperplasia of the ventricular ependyma at the site of the porus. While some thickening of the ependyma has been mentioned by various authors,

17. Strümpell, A.: Ueber die akute Encephalitis der Kinder, Jahrb. f. Kinderh. **22**:173, 1884.

18. Von Limbeck, R.: Zur Kentness der Encephalitis cong. in ihrer Beziehung. z. Porencephalie, Ztschr. f. Heilk. **7**:87, 1886.

19. Globus, J. H.: Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

20. Winterode, R. P., and Lewis, Nolan D. C.: A Case of Porencephalic Defect Associated with Tuberculous Encephalitis, Arch. Neurol. & Psychiat. **10**:304 (Sept.) 1923.

only the report by Schultze [21] mentions a similar condition. There has been much discussion about the "Körnchenzellen." Schwartz, Siegmund and Fischer [22] consider them pathologic, and Fischer believes that they are a sequence of trauma at birth. Lubarsch [23] doubts that they have any pathologic significance. Wohlvill regards fat infiltration in the glia cytoplasm physiologic up to the fifth month, and Lubarsch, Aschoff and Fischer are of the same opinion. Calcification of the cerebral arteries and lime concrements lying loose in the subependymal tissues are also reported by Freeman [24] in a case of tuberous sclerosis in a child 6 years old. Schmincke [25] found such changes in two cases of encephalitis in children 9 and 19 months old. Dürck,[26] in acute encephalitis, found marked calcification in varying degrees in twelve out of fifteen cases, lime incrustation of ganglion cells, free lime débris in the brain tissue and calcification of the vessel walls. Herzog [27] found calcification of the cerebral arteries four days after death from carbonmonoxid poisoning. Dense lime deposits in the capillaries of the white matter and basal ganglia are also described by Bassoe and Hassin,[28] who consider it the result of some nerve intoxication.

Ependymal tumors are not of frequent occurrence. Bailey [29] described six cases from Cushing's collection of 868 tumors. Boveri [30] demonstrated five brains from the clinic of Pierre Marie, with multiple, hard projections on the ventricular ependyma the size of a lentil composed of neuroglia. Branca and Marmier [31] from a histologic examina-

21. Schultze, F.: Beitr. z. Lehre von den angebornen Hirndefekten (porencephalie), Heidelberg, 1886.

22. Schwartz; Siegmund, H., and Fischer, B.: Centralbl. f. allg. Path. und path. Anat. **33**:588, 1923.

23. Lubarsch, O.: Centralbl. f. allg. Path. und path. Anat. **33**:588, 1923.

24. Freeman, W.: Tuberous Sclerosis, Arch. Neurol. & Psychiat. **8**:614 (Dec.) 1922.

25. Schmincke, A.: Enceph. Interstitialis (Virchow) mit Gliose und Verkalkung, zugleich im Beitr. 3. Verkalkung intracerebraler gefasse, Ztschr. f. d. ges. Neurol. u. Psychiat. **60**:290, 1920.

26. Dürck, H.: Ueber die Verkalkung von Hirngefässen bei der akuten Encephalitis lethargica, Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:179, 1921.

27. Herzog, G.: Zur Path. der Leuchtgas Vergiftung mit makro. und mikros. demonstrationen, Med. Wchnschr. **67**:558, 1920.

28. Bassoe, P., and Hassin, G. B.: Calcification of the Cerebral Vessels with Clinical Picture Simulating Brain Tumor, Arch. Neurol. & Psychiat. **6**:359 (Oct.) 1921.

29. Bailey, P.: A Study of Tumors Arising from Ependymal Cells, Arch. Neurol. & Psychiat. **11**:1 (Jan.) 1924.

30. Boveri: Ueber eine besondere und wenig bekannte Läsion des ventriculären Ependyms, Neurol. Zentralbl. **27**:887, 1908.

31. Branca, A., and Marmier, R.: Contribution â l'étude des malformations épendymaires, Bibliog. Anatom. **23-24**:279, 1913-1914.

tion of eight embryos give the following classification of ependymal anomalies: simple malformations; malformation combined with inflammation, tuberculosis, myelitis, tumors, etc.; malformation with medullary heterotopic lesions, and congenital lesions. According to Frank,[32] subependymal gliosis may give rise to true proliferating tumors just as malformations do in other organs. The difference between the hyperplasia of the neuroglia cells and glioma has been brought out by Ströbe,[33] Formerly the name diffuse hypertrophy was given to glia tumors, but, according to Uyematsu,[34] glia tumors and gliosis are influenced by the same stimuli. This author found gliosis in parts far removed from the tumor; he believes that glioma is formed from displaced embryomic tissue by a group of neuroglia cells of unstable character. Thomas and Jumentié [35] also described coexistence of glioma with granular ependymitis, the small ependymal nodules being in all respects comparable to glioma. Evidently no histologic examination was made by Schultze,[21] and the author contents himself with stating that the ependyma was variably thickened by wartlike projections. This hyperplasia may possibly be the result of a long standing arterial hyperemia, and similar changes have been produced experimentally in muscle tissue after tenotomy (Ricker [36]). In almost all cases of porencephaly, we see more or less disarrangement and lessening in number of the pyramidal cells in the cortex adjoining the porus, with replacement of such cells by glia cells and fibrils. All other changes apparently depend on the origin of the defect, whether inflammatory, ischemic, or traumatic. If the defect is extensive and involves important communication or relay centers, we find signs of agenesis or atrophy in other parts of the brain, medulla and spinal cord; but if only small portions of so-called silent areas are affected, the changes are confined entirely to the site of the porus. When there is no contact between the motor cell of the spinal cord with the extension of the neuraxon of the cortical pyramidal cells, the motor cell will be poor in chromatin and have the aspect of spongioplasm (Solovtzoff [37]). In view of the nodular hyperplasia of

32. Frank, A.: Ueber subependymäre Glia-Knoten, Frankfurter Ztschr. f. Path. **14**:450, 1913.

33. Ströbe, H.: Ueber Entstehung und Bau der Hirngliome, Beitr. z. path. Anat. u. allg. Path. **18**:405, 1895.

34. Uyematsu, S.: Contribution to the Study of Glioma, J. Nerv. & Ment. Dis. **53**:81, 1921.

35. Thomas, A., and Jumentié, J.: Gliome infiltré du lobe temporal droit, Rev. neurol. **29**:1525, 1922.

36. Ricker, G.: Beitr. zur Lehre der Atrophie und Hyperplasie, Virchow's Arch. f. path. Anat. **165**:263, 1910.

37. Solovtzoff, N.: Sur les deformités congénitales du cerveau, Nouvelles Iconogr. de la Salpétrière de Paris **11**:185, 1898.

the ependyma in this brain, it is of interest to comment briefly on what others have noted as to the relationship between such benign overgrowths of neuroglia and gliomas, a relationship long considered in other tumors.[38]

Theories as to the cause of glioma are abundant. According to Ribbert,[39] the origin may be from glia cells or from cells behind in development, the so-called spongioblasts. These tumors are variable in structure, some with well formed and regularly distributed astromes, others with large cells rich in protoplasm resembling ganglion cells, still others rich in fibrillar stroma and small spindle-shaped cells, and finally gliomas entirely composed of cells with hardly any fibrils and with a sarcoma-like appearance. These have been wrongly called glio-sarcomas. Ribbert believes the time of origin may be judged by the preponderance of cells or of fibrils, the tumors rich in cells starting at an earlier stage of development than those rich in fibrils, the more embryonal in character the earlier the onset of the growth. Gliomas may start during embryonic life (Eulenburg [40]), and, owing to their slow growth give no symptoms until many years later (Ewing [41]). Golgi [42] is of the opinion that the characteristics of the tumor cells correspond to those of the glia cells where the tumor originates, astromes with short projections with gliomas from the gray matter, and glia cells with long projections in gliomas from the white substance. Ströbe's theory of a parasitic origin of glioma based on sporozoae-like incrustations in the tumor cells of two of his cases is emphatically opposed by Muthmann and Sauerbeck,[43] who have been unable to find anything similar; neither do they believe in trauma as a cause, although they think that it may stimulate the growth of an already existing tumor. Ramon y Cajal [44] is of the opinion that neuroglia having power of proliferation responds to inflammatory stimuli by filling out the space of degenerated or necrotic nerve cells, and this view is supported by a number of authorities. In brains with cerebral thrombosis, del Rio Hortaga [45] found groups of cells which he believed to be emigrated ependymal cells, and in instances

38. LeCount, E. R.: The Genesis of Carcinoma of the Fallopian Tube in Hyperplastic Salpingitis with Report of a Case and a Table of Twenty-One Reported Cases, Bull. Johns Hopkins Hosp. **12**:126, 1901.

39. Ribbert, H.: Ueber das Spongioblastom und das Gliom, Arch. f. path. Anat. u. Physiol. **225**:195, 1918.

40. Eulenburg, A.: Realenzyklopädie der gesammten Heilk. **8**:464, 1886.

41. Ewing: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1919, p. 392.

42. Golgi: Ueber Gliome des Gehirns, Jena, 1884.

43. Muthmann and Sauerbeck: Ueber eine Glia-Geschwulst des IV Ventrikels, Beitr. z. path. Anat. und z. allg. Path. **34**:455, 1903.

44. Cajal, y Ramon: Histologie du système nerveux de l'homme et des vertébrés **1**:215, 1911.

45. del Rio Hortega, cited by Bailey, footnote 29.

of ependymitis he followed their transformation into glia cells. Müller [46] described five brains with scars from trauma mostly composed of glia cells and only to a slight extent of cells of mesenchymal origin. That the glia cell responds invariably to every sort of stimulation with exactly the same form of reaction and proliferation, is the view of von Podmaniczki.[47] Pedro y Cajal [48] asserts that the normal epithelial cells and astrocytes during embryonic life and after birth are capable of proliferation under normal circumstances. Disseminated gliosis was found with all gliomas studied by Uyematsu, and, in his opinion, there is a common causative factor for glioma and general gliosis. Winkler,[49] on the other hand, is just as confident that there is no relationship between glioma cells and the reactive glia; in fact, there is supposed to be a definite distinction between these cells based on histologic differences in structure and behavior. It seems therefore that investigations so far have led to a variety of interpretations which make it difficult at present to form an opinion based on sufficiently reliable data. Whether or no glioma and hyperplasia of the neuroglia are closely related requires further investigation.

We believe that the porus in Cases 3 and 4 are congenital and due to an inflammatory process; that in Case 1 it was caused by an ischemic necrosis and in Case 2 by trauma; also that porencephaly is the final result, as a rule, of vascular, traumatic and inflammatory processes, mostly produced during fetal life; and that the initial cause, if ascertainable, must be learned from a painstaking study of each brain presenting such alterations.

CONCLUSION

Porencephaly may be congenital or acquired. The anomaly is not inconsistent with life, in fact the individual with such a brain may live many years without any sign or symptom of the lesion. In other instances, there may be marked disturbances of motor function or mentality, or the condition may cause death shortly after birth. This wide range of sequences is apparently altogether connected with the site and extent of the defect. With porencephaly there may be dystrophy and agenesis in remote parts of the brain, pons, medulla and spinal cord.

46. Müller: Ueber die Beteiligung der glia an der Narbenbildung im Gehirn, Deutsch. Ztschr. f. Nervenh. **23**:296, 1902-1903.

47. Von Podmaniczki: Concerning the Role of Glia in Diseases of the Cortex of the Cerebrum, Arch. f. Psychiat. **59**:281, 1918.

48. Cajal, Pedro y: Trab. de lab. de investig. biol., Univ. de Madrid **11**:255, 1914.

49. Winkler, Junius: Einige obmerkingen over de histogenese van het glioma cerebri en over het verschil in histologische bouw tuschen gliomweefsel en reactive neuroglia, Psychiat. en Neurol. Blad. **24**:198, 1920.

THE WEIR MITCHELL REST CURE FORTY YEARS AGO AND TODAY*

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In these so-called modern days, it is the fashion to look with scorn at any method of treatment or diagnosis which is more than a few years old. A book published five years ago is out of date. An old method of treatment, no matter how good it may have been in the past, is regarded as antiquated.

Since Weir Mitchell first published his book, "Fat and Blood," in 1877, now forty-seven years ago, the osteopaths, chiropractors, napra-paths and a host of other "paths" have come into being. Then there are the Christian scientists, Bohemian thrusters, electrical specialists, and, in later years, the psychanalysts have come into fashion.

It would be wrong to place psychanalysis in this group, were it not for the fact that psychanalysis has graduated from the ranks of medical men and is now being practiced by persons not at all trained in medicine, most of whom are as poorly equipped to treat disease as some of those who practice the various sorts of "paths." It would be difficult to classify these cults better than was done by Weir Mitchell, who stated some years ago that all of them had this in common—a natural scorn for each other.

Psychanalysis of course rests on a firmer foundation. It has a legitimate basis, and in certain selected cases it is of value. But even psychanalysts, in their eagerness to treat the psyche of their patient, frequently forget the fact that the body perhaps needs an equal amount of care.

More recently the possibilties of endocrinology have captured the imagination of the medical public. To a large extent, the facts on which its physiology is based still remain a matter of conjecture. Still more recently, the doctrine of focal infection has come into vogue. On its altar, millions of teeth and thousands of tonsils have been sacrificed.

There is of course a modicum of truth in all of these beliefs. No one questions the brilliant results obtained by the judicious removal of focal infection, or proper glandular therapy. It is only necessary to quote insurance statistics which show that during the last ten years there has been a remarkable drop in the incidence of arthritis because of the

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removal of focal infections. Equally brilliant have been the results obtained by thyroid therapy in suitable cases.

It is fitting, therefore, that on this occasion we review a method of cure for the treatment of disease the success of which has been established by the experience and judgment of years.

In the concluding paragraph of his discussion of the "Rest Treatment" in his book, "Fat and Blood," [1] Weir Mitchell states:

> I am fortunate in having been able to show that in other hands than my own this treatment has so thoroughly justified itself as to need no further defense or apology from its author. I am now more fearful that it will be misused or used where it is not needed than that it will not be used; and with this word of caution I leave it again to the judgment of time and my profession.

The basis of the rest cure depends on the combined use of rest, isolation, overfeeding, massage and electricity. Up to Mitchell's time, all of these measures were used independently, but it was left to Mitchell to use them together, and thus attain the marvelous success which followed the inauguration of this method. For years after initiation of the treatment, Philadelphia was the Mecca for patients from all over the world, but during the last twenty years there has been a decrease of the use of this method, except by the older physicians and by those who are connected with the Infirmary for Nervous Diseases, where the rest treatment had its beginning.

Perhaps its lessened use is partly due to Mitchell's death, but it seems to me that the younger and present generation of physicians is not aware of its usefulness. With this point in view, I shall analyze from the so-called modern standpoint the reasons for its success.

It is a mistaken belief that Mitchell advised the rest treatment for most nervous patients. He emphatically states:

> *It is a plan never in my opinion to be used where exercise, outdoor life, tonics or change have not been thoroughly tested,* but where these have failed. . . . I never use it if I can do without it; but in well chosen cases I use it with a confidence which has become alike courageous and habitual.

He divided patients, for whom he advised rest cure, into two classes:

> *One,* the nervous and hysterical woman who is at the same time fat, but has a real anemia. These patients are more or less feeble, not large feeders and prone to suffer from excessive tire upon disproportionate exertion; *second,* the large group of nervous excited patients who are as a rule weak, pallid, with rough, coarse skins, poor digestion, who suffer with cold extremities and are anemic; in other words, the so-called cases of nervous exhaustion.

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1. Mitchell, Weir: Fat and Blood, Philadelphia, J. B. Lippincott Company, 1900.

The rest cure has its value in cardiac cases with lack of compensation, in goiter and similar conditions. Mitchell also advised its use in true melancholia, especially in the agitated state.

Whether he prescribed absolute or partial rest, depended on the physical and mental condition of the patient. The length of the treatment also varied. Usually the patient had absolute rest for from six weeks to two months, and was then allowed out of bed for gradually increasing periods.

The rest treatment does not mean that a patient is taken away from his home and placed in a room in the care of a nurse, overfed and given massage and electric treatment. While physicians appreciate the benefits of rest, not all are aware of the value of isolation. It means that the patient is taken away from the environment which perhaps contributed to his undoing, and is removed from the vexations and irritations of home life, which in large part cause the various nervous symptoms already established to continue. This in itself is of distinct benefit. After the patient goes to the hospital, he is thoroughly studied from every angle. In other words, the patient is given the benefit of a so-called "diagnostic clinic," and medical treatment is instituted according to the needs of the patient. The only difference between the method as it is practiced now and as it was practiced in Mitchell's time is that we have the additional advantage of a more modern laboratory and its refinements of biochemistry and serology, and the benefits of roentgen-ray diagnosis and treatment.

Mitchell paid the greatest attention to the diet. He was in the habit of placing the patient on a milk diet, at least at first, gradually substituting the particular diet which the patient's needs called for, and later resorting to overfeeding so that weight could be gained.

It is equally difficult for a patient to gain and lose weight, but in most instances it is more important for the patient to gain. One of the outstanding features noticeable in the course of rest treatment is the general improvement in the physical and mental well-being of the patient as there is a gradual increase in weight.

His use of a milk diet, at least in the beginning of the treatment, had a sound physiologic basis, for it not only gave the gastro-intestinal system a chance to right itself, but it was in reality a forerunner of the modern method of changing the flora of the gastro-intestinal tract by the administration of bacterial cultures.

Mitchell was aware of the fact that he could not overfeed his patient without at the same time exercising his body, so he resorted to massage and electricity. Up to his time, massage had been used by charlatans, and it remained for him to standardize its use.

Some physicians will be surprised to find the following advice:

> It is a remedy with the capacity to hurt as well as to help and should never be used without the advice of the physician nor persistently kept up without medical observation of its temporary and more permanent effects.

He was insistent that the sensitive spines and sore spots in the back be carefully rubbed out by means of massage, and in discussing its use, in 1899, he stated:

> I never could see why a tonic so valuable as this should be left to assist the triumphs of the charlatan; and I feel that, in making it of easy use, I have done that which, in many ways, is valuable to the surgeon and the physician.

I have no doubt that had Mitchell's advice been heeded, the modern cults of osteopathy, chiropathy, naprapathy and Bohemian thrusters would never have existed. Mitchell also introduced to physicians the use of hydrotherapy and external heat, although he was probably not the first to use it. Dr. Charles W. Burr, who for years was associated with Mitchell, states that Dr. Simon Baruch of New York was the first to practice these measures, and that he was regarded by many as a charlatan. It was not until Mitchell took this method in hand and made it popular that its use was generally accepted by physicians. The universal use of external heat and hydrotherapy has abundantly justified Mitchell's broadness of mind. Recently Pemberton and his co-workers have shown that the benefit of the so-called electric cabinet bakes is attained through the heightened blood flow coincidently with the elimination of acids, chiefly carbon dioxid, through the lungs, urine and perspiration—named in order of magnitude.

As to the benefits of massage, Mitchell's ideas have been substantiated by Philadelphia investigators. In 1894, John K. Mitchell showed that in health and anemia, massage increased the number of red cells, and that especially in anemia the increase is greatest after an interval of one hour, beyond which it slowly decreases.

In five patients to whom vigorous massage was given, Pemberton [2] (in association with Cajori and Crouter) studied the hydrogen-ion concentration, carbon dioxid content, oxygen content, oxygen capacity, percentage oxygen saturation, inorganic phosphorus and lactic acid of the venous blood before and after massage, and also the hourly volume, titratable acid, organic acids and inorganic phosphorus of the urine before and after massage. It was noticeable that neither in the venous blood nor in the urine did any of those changes take place which characterize the acid swing of active exercise or the acid elimination and

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2. Pemberton, Ralph; Cajori, F. A., and Crouter, C. Y.: The Physiologic Effect of Massage, J. A. M. A. **83**:1761 (Nov. 29) 1924.

alkaline swing following the exposure of the body to external heat. This absence of demonstrable chemical changes to account for the benefits of massage, according to Pemberton, gives added emphasis to the mechanical effects accompanying it; and he came to the conclusion that massage causes a change in the peripheral circulation, especially capillary, whatever the precise mechanism involved. This is further indicated by the small but consistent rise in the oxygen capacity of the blood in all the cases studied by him, and also by the increase in the red cell count.

ELECTRICITY

While Mitchell regarded the use of massage as absolutely essential, he was not as insistent on the use of electricity. It involved the daily use of induction currents, with slow interruptions, to almost every muscle which could be reached, the object being to throw each muscle into decided contraction. Finally, a mild current with rapid breaks was made to pass from the neck to the feet for fifteen minutes. He regarded its use as a powerful tonic. Not much work of the character quoted above has been done to ascertain the physiologic effects of electricity, but as its object is to obtain muscular contraction, the chances are that its benefits are like those of massage.

One of the chief arguments used against the efficiency of the rest treatment is that while the body is looked after, the mental symptoms are neglected, in fact, are made worse by the isolation. This argument, to any one who came in personal contact with Weir Mitchell, is at once recognized as specious. The great success which Mitchell attained was in large part due not only to the physiologic benefits resulting from the treatment, but also to his ability to understand and adjust social and mental problems, which nearly always underlie nervous phenomena. In his writings, he comments on the sexual element in the symptomatology of his patients. He emphasized the necessity of the careful study of the patient's character, home surroundings and incidents of social life which come with the development of "possible passion." Elsewhere he discusses the chain of circumstances, of love affairs and disappointments, and it is not surprising that he states:

> I look upon most cases of confirmed hysteria as finally dependent upon physical defects which may have been directly or indirectly due to moral causes, or these in conjunction with constitutional conditions.

Mitchell had the good sense not to attack the mental phase of his patients until they were better physically, for many of the disturbing mental problems gradually disappear in the process of physical well-being. Besides, during the period of rest treatment, the patient, who is altogether under the control of the physician, can be abundantly

analyzed, and the mental and moral states adjusted. It is obvious from the foregoing that Mitchell practiced psychanalysis and recognized that hysterical symptoms can result from mental causes. In addition to a scientific knowledge of mental and nervous phenomena, he had what many psychanalysts do not have, a large understanding and a wide grasp of social problems, which enabled him to adjust the patient to his environment.

To any one who is at all familiar with Mitchell's writings and work, it is obvious that he had a broad grasp of physiologic problems, and that the development of his rest cure was not the result of chance. A perusal of his early writings shows that he was a physiologist, and it is not a secret that he at one time aspired to the position of professor of physiology in one of our medical colleges.

At this fortieth anniversary of the foundation of the Philadelphia Neurological Society, it is an honor to tell of the work of the first president of the Society, and fitting to call the attention of the modern medical public to the achievements of one of its most distinguished members, who inaugurated a method of treatment which, if properly used, is just as valuable today as it was at its inception more than forty years ago.

CEREBROSPINAL FLUID SUGAR*

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This preliminary report on the cerebrospinal fluid sugar is based on the study of 425 spinal fluid and 150 whole blood or plasma sugar determinations made at the Massachusetts General Hospital during the past year. Folin and Wu's latest modification for blood sugar [1] was the method used, the spinal fluid protein-free filtrate being prepared as recommended for blood plasma. The final dilutions were made in the modified sugar tubes recommended by Rothberg and Evans.[2] Methods will be discussed in a later communication.

In 1852, Deschamp and Bussy [3] found a reducing substance in the cerebrospinal fluid escaping from the ear of a patient with fractured skull. In 1897, Nawratski [4] proved conclusively that this substance was glucose.

The relation of spinal fluid sugar to blood sugar has been a disputed subject. That the spinal fluid sugar is high and sometimes equals the blood sugar in diabetes mellitus is well known. Several investigators [5] during the past five years have shown in dogs and rabbits that the spinal fluid sugar follows blood sugar changes after a latent period.

On the nature of the relation to the blood sugar in man there is little agreement. For example, Wittgenstein,[6] in 1923, concluded that the spinal fluid sugar level is independent of the normal fluctuations of the blood sugar, the spinal fluid sugar representing from 50 to 80 per cent. of blood sugar, while Polonovski and Duhot [7] found blood and spinal

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1. Folin, O., and Wu, H.: J. Biol. Chem. **41**:367, 1920.

2. Rothberg, V. E., and Evans, F. A.: J. Biol. Chem. **58**:435 and 443, 1923-1924.

3. Deschamp and Bussy: Bull. de l'Acad. nat. de méd. **18**:240, 1852.

4. Nawratski, E.: Ztschr. f. physiol. Chem., Strassburg **23**:532, 1897.

5. Ino, I.: Actae scholae medicinalis, univ. imp. Kioto **3**:609, 1920. Kimura, N.: Japan Med. World **3**:67, 1923. Kasahara, M., and Uetani, E.: J. Biol. Chem. **59**:433, 1924. Kubie, L. S., and Schultz, G. M.: J. Exper. Med., in press.

6. Wittgenstein, A.: Deutsch med. Wchnschr. **49**:246, 1923.

7. Polonovski, M., and Duhot, E.: Presse méd. **31**:60, 1923.

fluid sugar values parallel and sometimes identical, both fasting and following hyperglycemic and hypoglycemic reactions. The blood sugar was usually higher than the spinal fluid sugar. They used a special method of protein precipitation, hoping thus to get rid of possible non-dialyzable portions of the blood sugar which they suggested might account for the higher blood sugar figures.

The idea that the reducing substances in the blood may not be all glucose is not new. In 1922, Folin and Berglund [8] concluded from the results of hydrolysis on the sugar content of whole blood and plasma filtrates that there are present in the blood, more especially in the plasma, reducing substances which disappear after hydrolysis, and therefore cannot be glucose. This nonglucose fraction at times amounted to over 10 per cent. of the so-called blood sugar.

That an appreciable fraction of the total reducing substance which we measure as blood sugar is not glucose complicates the study of the relation of blood sugar to spinal fluid sugar and at once raises the question whether all the spinal fluid reducing substance is glucose.

In twenty-five instances we have hydrolyzed spinal fluid filtrates using Folin and Berglund's technic. In the majority of the cases the spinal fluid sugar values have decreased after hydrolysis, this nonglucose fraction varying from 1 to 15 per cent. of the total. In a few instances the sugar content increased. In the blood specimens our results were similar to those of Folin and Berglund, the change in sugar content of blood and spinal fluid usually being parallel. Further studies are in progress.

This indicates that in the spinal fluid as well as in the blood plasma there are usually present reducing substances other than glucose, which may disappear on hydrolysis and which may amount to more than 10 per cent. of the total measured spinal fluid sugar.

In the few cases in which lumbar and ventricular fluids have been obtained, simultaneously, fasting, we have found the sugar in the ventricular fluid somewhat higher than in the lumbar. This agrees with the observations of Céstan, Riser and Laborde.[9] The cause of this difference has not been established. The higher ventricular values favor the view that cerebrospinal fluid contains its sugar as it is formed in the ventricles.

The sugar content in the ventricular fluid, although somewhat higher than that in the lumbar fluid, is not as high as the blood sugar. That the blood sugar is nearly always higher than the spinal fluid sugar is one point on which most observers agree. The nonglucose fraction of

8. Folin, O., and Berglund, H.: J. Biol. Chem. **51**:213, 1922.
9. Céstan, Riser and Laborde: Rev. neurol. **39**:353, 1923.

the plasma sugar does not account for the difference since that fraction may be present in the spinal fluid in about the same percentage as in the blood plasma. The explanation for the higher blood sugar is not forthcoming at present. It is possible that the cells of the choroid plexus utilize a portion of the sugar transmitted through them.

The weight of evidence, then, indicates that the spinal fluid sugar is derived from the blood sugar and is in some way dependent on it. This may be accepted in the absence of evidence to the contrary.

It will be seen that if the spinal fluid with its sugar content is formed in the ventricles, the speed with which the ventricular fluid will reflect blood sugar changes will depend in part on the rate of formation of the fluid. On this point no reliable data is at hand, but it is probable that the hourly production in man is somewhere between 5 and 30 c.c. A transient high blood sugar can directly affect only that portion of the cerebrospinal fluid which is newly formed during the hyperglycemic period. The ventricular fluid formed during such a period, with its higher sugar content, must then be mixed with fluid previously and subsequently formed, and after an unknown period, depending on the fluid circulation and diffusion rate, reach the lumbar sac. It will not be surprising, then, to find little immediate change in the sugar content of the lumbar fluid following rather definite blood sugar increases. The investigators [5] already referred to observed a latent period in dogs and rabbits even though the fluid was removed from the cisterna magna.

We have obtained simultaneous spinal fluid and blood samples during sugar tolerance tests on four patients—three with epilepsy and one with degenerative disease of the cord. The glucose was given once intravenously and three times by mouth. In the latter cases the spinal fluid sugar rose only 3, 4 and 6 mg. per hundred cubic centimeters, respectively, during a period of fifty minutes, while the plasma sugars rose from just above 90 to 144, 160 and 162 mg. When the glucose was given intravenously, the plasma rose from 111 mg. fasting to 290 mg. at the end of ten minutes, and then gradually fell. The spinal fluid collected at intervals of ten minutes showed no appreciable change for seventy minutes, at which time the blood sugar had fallen to 140 mg. Twenty minutes later, or one and one-half hours after the intravenous injection of glucose, the spinal fluid sugar had increased a total of 9 mg., while the falling plasma sugar had reached 99 mg., which was 10 per cent. lower than at the beginning of the test. It should be remembered that such slight rises in spinal fluid sugar are no greater than normal differences between lumbar and ventricular sugar, and as a considerable quantity of fluid is removed during such a test, the last sample may represent fluid which was in the ventricular system at or near the beginning of the test.

DELAYED RESPONSE TO BLOOD SUGAR CHANGES

This indicates that for an hour or more after the administration of glucose, hyperglycemia is not accompanied by a significant rise in the lumbar spinal fluid sugar. That the lumbar fluid sugar does, however, respond to blood sugar changes in man after a latent period is indicated by the results of sugar tolerance tests continued over a period of several hours. These will be reported in detail in a subsequent paper. The following case is an example of such delayed response to blood sugar changes:

A boy, aged 12 years, with acute nephritis, had a series of convulsions beginning at 7 a. m. Blood was taken at 9 a. m. during the seizure—the sugar content was 312 mg. per hundred cubic centimeters. A little later the convulsions ceased. At 1 p. m., the blood sugar was 200 mg., while at 4:30 p. m. the plasma sugar was 122 mg. Spinal fluid withdrawn at this time had a sugar content of 136 mg., appreciably higher than the plasma. Without the knowledge of the earlier marked hyperglycemia, we should have been at a loss to understand a spinal fluid sugar 10 per cent. higher than the coincident blood sugar.

A few days later, the patient had more convulsions. Blood taken at the onset showed a sugar content of 174 mg. Two hours later, during the convulsion, the plasma sugar was 319 mg. Lumbar fluid taken at this time showed a sugar content of 107 mg. Here we have in the same patient on one occasion a spinal fluid sugar of 136 mg. with a coincident plasma of 122 mg., a few days later a spinal fluid sugar of 107 mg., while the plasma sugar is 319 mg. In the first instance, we had a rapidly falling blood sugar which had been very high, in the second, the blood sugar had climbed to 319 mg. within two hours and the spinal fluid sugar had had but little time to respond. The fasting blood sugar content in this patient on other days was normal.

SPINAL FLUID SUGAR CONTENT IN VARIOUS CONDITIONS

It is necessary to know the blood sugar values, preferably the plasma sugar value, since it is from the plasma that the interchange takes place, not only at the time of the lumbar puncture, but also for an as yet unknown period preceding the withdrawal of fluid, before we can reach conclusions in regard to the normal relationship between blood and spinal fluid sugar.

The lack of consideration of these various factors and our present imperfect knowledge of the relationship of cerebrospinal fluid sugar to blood sugar, whence it is derived, explains the disagreement in the literature as to the normal spinal fluid sugar values, which range from 50 to 134 mg., as given by Schloss and Schroeder in 1916,[10] to much narrower limits, as 55 to 65 mg. set by Mestrezat [11] in a paper published a few months ago.

10. Schloss, O. M., and Schroeder, L. C.: Cerebrospinal Fluid, Am. J. Dis. Child. **11**:1 (Jan.) 1916.

11. Mestrezat, W.: Ann. de l'Inst. Pasteur **38**:719, 1924.

Of 318 spinal fluids from cases wherein the diagnosis was established, fifty-seven had sugar values between 80 and 160 mg. With twenty-one of these simultaneous blood sugars were determined, and in twenty the sugar content was high. This indicates that hyperglycemia rather than central nervous system changes was responsible for the high spinal fluid sugar content. The diagnosis in this group included such varying conditions as brain tumor, brain abscess, uremia, carbon monoxid poisoning, epidemic (lethargic) encephalitis, meningismus, cerebral vascular accidents, syphilis of the central nervous system, fluid removed under ether and fluid obtained after intravenous injection of glucose. Sixty-four fluids had a sugar content below 50 mg., and of these fifty-nine were cases of acute meningitis, including tuberculous and acute purulent syphilitic meningitis. In the five remaining fluids with a low sugar content, there were marked cellular reactions. In seven of this group with a sugar content below 50 mg. coincident blood sugar ranged from 99 to 155 mg. per hundred cubic centimeters, indicating that these low spinal fluid sugar contents were independent of the blood sugar level. This is in accordance with the findings of Kelley,[12] who showed that inoculation of spinal fluid with bacteria and subsequent incubation caused the sugar to diminish.

The remaining 197 fluids, with sugar contents varying from 50 to 80 mg., were also obtained in a variety of conditions, such as syphilis of the central nervous system, brain tumor and abscess, early tuberculous and early acute purulent meningitis, poliomyelitis, epidemic (lethargic) encephalitis, and cases in which there was no evidence of disease of the central nervous system. In these cases simultaneous blood sugar was obtained in forty-nine cases, only seven being above 125 mg. We are unable to say that any of these cases are normal, although we feel that normal fasting values will fall within this group. At a later date, we shall present data on fasting blood and spinal fluid sugar.

The diagnostic significance of the sugar content in cerebrospinal fluid will be discussed in our paper on cerebrospinal fluid chlorids.[13]

CONCLUSIONS

1. Spinal fluid, as well as blood plasma, contains reducing substances other than glucose, which disappear on hydrolysis and which may amount to more than 10 per cent. of the total measured "sugar" content.

2. The hyperglycemia produced by sugar tolerance tests is reflected in the lumbar spinal fluid only after a latent period following the admin-

12. Kelley, A. G.: Southern M. J. **16**:407, 1923.

13. Fremont-Smith, F., and Dailey, M. E.: Arch. Neurol. & Psychiat., in press.

istration of glucose, by which time the blood sugar may have fallen to below the spinal fluid sugar level.

3. Because of these facts no statement can be made at present as to the normal ratio of spinal fluid sugar to blood sugar, nor can the normal limits of spinal fluid sugar be given.

4. Spinal fluid sugar contents above 80 mg. occur in a great variety of conditions as well as in epidemic (lethargic) encephalitis. Such values are usually associated with hyperglycemia, which is not uncommon in cerebral conditions.

5. In the absence of hypoglycemia, spinal fluid sugar contents below 50 mg. nearly always indicate an acute infection of the meninges.

6. Sugar values in the cerebrospinal fluid between 50 and 80 mg. occur when no pathologic condition of the central nervous system exists, but may also be found in such differing conditions as early acute meningeal infections, epidemic (lethargic) encephalitis or brain tumor.

7. Spinal fluid sugar should be determined on patients fasting, preferably over night, and compared with coincident blood sugar.

Clinical and Occasional Notes

GLIOMA OF THE BULB AND PONS

A REPORT OF FOUR CASES *

PETER BASSOE, M.D., AND C. W. APFELBACH, M.D., CHICAGO

Though anatomically similar, these cases presented dissimilar and variable clinical pictures, with predominance of distant symptoms produced by secondary hydrocephalus. A correct clinical diagnosis was definitely made only in the first case, and it was made by means of pneumoventriculography. In this case, inflammatory disease of the frontal region had at first been suspected. In the second case, serous meningitis following a throat infection was at first suspected. Later, a stage of decerebrate rigidity developed and lasted for many months. The third case was considered one of encephalitis of the brain stem, as the general symptoms of brain tumor were lacking. In the fourth case, a lesion of the pons was obvious, but it was a question whether the lesion was neoplastic or inflammatory.

REPORT OF CASES

CASE 1.—*History.*—For the early history we are indebted to the patient's family physician, Dr. A. N. Wiseley of Lima, Ohio.

A married woman, aged 24, was admitted to the Presbyterian Hospital on Jan. 16, 1924.

In 1920, a therapeutic abortion was performed after an acute abdominal affection, thought to be appendicitis, had been followed by signs of kidney disease and persistent headache. During a second pregnancy, resulting in normal delivery in July, 1922, there was much nausea and vomiting. In the fall of 1922, she had three or four attacks of severe headache lasting from one-half to one day. In February, 1923, she had an attack of what was considered influenza, with fever, severe headache and pain at the back of the neck. The fever lasted only a few days, but the headache and "drawing" pain in the neck continued, and after a month, blurring of vision set in, with diplopia for a couple of days. Vomiting and marked retraction of the neck often occurred during severe attacks of pain. On March 23, 1923, lumbar puncture yielded a clear fluid under increased pressure, with a negative Wassermann reaction but a positive Noguchi globulin test, and a cell count of 160. The eyegrounds at that time were recorded as "practically negative." A second spinal examination in May, 1923, gave a count of 200 lymphocytes. There were occasional attacks of dysphagia lasting two or three days. Vomiting was frequent, sometimes projectile, sometimes accompanied by nausea. The pain was most severe in the forehead and at the back of the neck. A third lumbar puncture was made about Sept. 1, 1923. The pressure and cell count were not increased; the globulin test was positive; the Lange gold test "did not indicate syphilis," and the Wassermann test again was negative. For some months in the fall, the headache was less severe, and the patient gained in strength. There was no more dysphagia, but blurring of vision continued. In December, papilledema was noted, and the patient had

* From the Neurological Service and Pathologic Laboratory of the Presbyterian Hospital, Chicago.

* Read at the meeting of the Chicago Neurological Society, Nov. 20, 1924.

difficulty in recognizing people's faces. On Jan. 14, 1924, swelling of 2 diopters in each eye, blindness of the right eye and ability to count fingers at 3 feet with the left eye were the findings. There was no paralysis of the external eye muscles; smell and hearing were normal. The rhinologic examination indicated posterior ethmoiditis and sphenoiditis.

Examination.—Condition on admittance Jan. 16, 1924: The patient was slender, poorly nourished, pale, normal mentally. Both pupils reacted to light, both directly and consensually. There was no paralysis of the cranial nerves or extremities. The corneal and pharyngeal reflexes were present; the plantar reflexes were normal; the abdominal reflexes were normal on the left, and diminished on the right; the tendon reflexes were normal. There was slight incoordination, especially of the upper extremities.

Course of Illness.—On January 17, lumbar puncture was performed. The pressure was 17 mm. of mercury; the Wassermann test was negative; the cell count was 6; the Ross-Jones globulin test was positive; the result of the Lange gold test was 0002221000. Smears and cultures were negative for bacteria. The blood count was normal. The blood pressure was: systolic, 100; diastolic, 78.

Dr. Edwin McGinnis reported purulent discharge from the right superior meatus and left middle meatus, marked deflection of the septum to the left and small atrophic tonsils with pus expressed from the right one. On January 18, he resected the septum and performed bilateral ethmoidotomy. Thick pus exuded from the anterior ethmoid cells on both sides.

January 21: There was loss of vision in the right eye; with the left eye, in a greatly narrowed field, the patient could count fingers at a distance of 1 foot. There was bilateral choked disk, 3 diopters swelling and a few small hemorrhages.

Spinal puncture was again performed on January 22. The pressure was increased; the cell count was 3; the globulin test was positive. The result of the Lange gold test was 0001321000. An hour after puncture, the patient complained of severe headache. The temperature, which had been practically normal at first, rose on January 2, and the patient passed through a light attack of bronchopneumonia which delayed for two weeks further study of the brain condition.

Vision in the left eye continued to decline, and on January 28 neither pupil reacted to light. On that day, lumbar puncture was again performed, and the pressure was 22 mm. of mercury. The cell count was 2, the Ross-Jones test positive, and the gold curve 0022321000.

February 2: Lateral stereoscopic roentgenograms of the head were taken. These showed marked erosion of the sella turcica and slight evidence of digital impressions.

February 4: Caloric tests showed that both horizontal canals reacted normally to warm water. The vertical and posterior canals reacted slowly, and less than the horizontal. The condition of the nose was satisfactory.

Clinical Diagnosis: By this time we were convinced that we were dealing with a tumor and not with an inflammatory condition. In spite of the erosion of the sella, we thought it most probable that we were dealing with a posterior fossa tumor involving the fourth ventricle rather than the cerebellum. We did not, however, want to risk a suboccipital operation without preliminary ventriculography.

February 11: Dr. Carl B. Davis made a trephine opening in the right occipital bone. Thirty cubic centimeters of clear fluid were removed, and a similar amount of air was injected. Roentgenograms were taken with the occiput, forehead and either side down against the films. That taken with the occiput down, allowing the air to rise to the anterior horns, showed both of these plainly.

In the lateral view, both ventricles were seen to be distended. The film taken with the forehead down showed air on the left side only, but as the puncture had revealed abundant fluid in the right posterior horn, this discrepancy was disregarded. No ill effect from this procedure was noted.

The patient was in a weak condition, had great difficulty in swallowing, and at times marked slowing of respiration. It was decided to perform a radical operation as soon as the condition permitted.

Feb. 28: Dr. Davis made a suboccipital operation. After exposing the cerebellum, a dark reddish growth was seen to project between the lobes. On dissecting the latter back, a tumor of more than walnut size was exposed, and a large part of it removed. The wound was closed. After the patient was removed from the table, the respirations became extremely shallow, and the patient died.

Anatomic Diagnosis: The anatomic diagnosis was: glioma of the medulla; internal hydrocephalus; recent cerebellar decompression; operation; cerebral hernia; recent partial removal of the tumor of the medulla; traumatic leptomeningeal hemorrhage of the pons and medulla; recent intranasal surgical operation; moderate general emaciation; erosion of the posterior clinoid process and posterior margin of the sella turcica; nodular, caseous tuberculosis of the tracheobronchial lymph glands; persistent thymus gland; multiple cysts of the kidneys; adenomas of the kidneys; slight fibrous external pachymeningitis; absent left ear drum.

When the scalp tissues were reflected, the cerebellum was exposed through a bony defect 10 cm. from side to side and 5 cm. up and down. A gauze drain extending through the vertical surgical incision extended under the cerebellum for 2 cm. in the midline, just above the pons. There was a round defect in the calvarium 9 cm. above and 2 cm. behind the upper attachment of the right ear. The calvarium except in a few places in the midline did not transmit light. The dura was slightly adherent to the inside of the cranium by easily torn fibrous adhesions. The convolutions of the top half of the brain were flattened; the sulci were obliterated, and the top half of the brain was pale gray. The medulla was enlarged and filled the upper end of the spinal canal. There was free blood in the soft meninges covering the ventral surface of the pons and medulla, in a space equal to about 6 to 7 square cm. The medulla was 3.5 cm. across; in the center of it, there was a cavity, but 5 cm. below the pons, the medulla again had its normal dimensions. Between the dorsal surface of the medulla and under surface of the cerebellum, there was a place in which the brain tissue and meninges were torn and in which there was a small amount of free blood in the tissue. This tear ran down toward the fourth ventricle. The posterior clinoid processes were small from erosion, so that the tips of each are a few millimeters below a horizontal plane through the tips of the anterior clinoid process. The posterior margin of the sella turcica was made up of fine spicules of bone. The pituitary body was flattened and 16 mm. wide, 14 mm. from front to back, and about 5 mm. thick. The floor of the sella turcica was made up of thin bone at the sides, front and back, and about two thirds of a fibrous membrane. In the floor of the right anterior fossa, about 1 cm. from the midline and 3 cm. in front of the sella turcica, the bone was light red-purple in a place 5 mm. across and 4 mm. from front to back. The lining of the sphenoid sinus and posterior ethmoid cells was smooth and shiny. In the middle ethmoid cells, there was some pink tissue, resembling granulation tissue and free blood. The lining of the frontal sinuses was smooth and shiny. The coverings of the right ear drum were intact; most of the left ear drum was missing. There was no pus here.

When the brain, hardened in formaldehyd solution, was opened by separating the cerebrum, cerebellum, pons and medulla into two equal lateral parts, a tumor was cut through that was attached to the floor of the fourth ventricle for 16 mm., the front end about 7 or 8 mm. inferior to the junction of the pons and medulla. This tumor had a maximum length of 28 mm. and a maximum height of 18 mm. The surfaces were light brown, mottled, with many dark red-brown spaces that resembled dilated blood vessels. The junction with the medulla was intimate, and there was a white band separating the two, from 1 to 2 mm. wide. The tumor pressed against the cerebellum, but did not grow into it; it was altogether dorsal to the medulla, its front margin at about the level of the recesses in the fourth ventricle leading to the cisterna. The tumor did not grow into the recessus tecti, but instead pushed the under surface of the cerebellum forward so that the recessus tecti sloped chiefly backward. The roof of the fourth ventricle inferior to the tumor followed the under surface of the tumor to its place of attachment

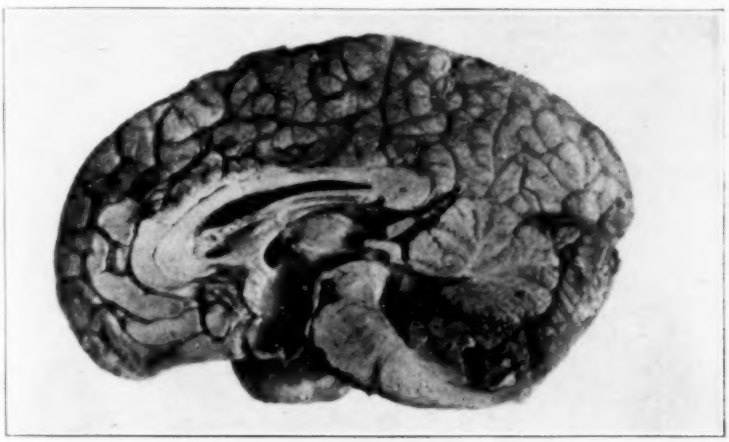

Fig. 1 (Case 1).—Sections made by cutting the brain into two equal parts showed a tumor attached to the floor of the fourth ventricle, pushing the cerebellum superiorly. There was marked dilatation of the third ventricle, aqueduct of Sylvius, and the upper one-half of the fourth ventricle.

in the floor of the fourth ventricle. The cavity of the inferior part of the fourth ventricle was entirely obliterated by the tumor. The tumor extended each way from the midline; at its middle, the maximum width was 22 mm. The surface was sharply demarcated from the under surface of the cerebellum, into which it pushed itself. The velum medullare posterior was not identified. In front of the tumor, the fourth ventricle was greatly dilated, so that in one half of the cerebral hemisphere, it was 15 mm. wide and 17 or 18 mm. high. The aqueduct of Sylvius was greatly dilated, and the third ventricle was from 5 to 6 mm. wide, 15 mm. high, just in front of the posterior commissure, and the part extending down toward the infundibulum was 16 mm. from front to back and 5 mm. from side to side. The lateral ventricles were enlarged. Distal to the tumor, the spinal cord was flattened so that it had a width of approximately 2 cm. and a thickness of not more than 4 or 5 mm., and this flattening extended down to the level of the foramen magnum.

Histology.—Almost half of the tumor was made up of large and small blood spaces, with thin walls, most of these spaces in the midst of abundance of glia fibers. Throughout the tumors there were areas poor in glia fibers and made up of masses of glia cells. They were surrounded by dense bands of glia fibers. The cytoplasm of the cells about equaled the nuclei in size. At the junction of the tumor and medulla, the band described grossly was made up chiefly of closely packed glia fibers. About some of the blood spaces, there was considerable connective tissue. In a few of the cell bodies, there were small granules. (Hematoxylin and eosin, and phosphotungstic and hematoxylin stains were used.)

Diagnosis.—Glioma.

Case 2.—*History.*—A girl, aged 6, was admitted to the Presbyterian Hospital, Dec. 14, 1922, on account of abdominal pain and vomiting which had existed for five weeks. Appendicitis had been suspected by the family physician. After four days, the child was discharged with a diagnosis of acute tonsillitis. On December 22, she was again admitted on account of recurrence of vomiting, this time associated with severe headache. The left eye was turned inward. Brudzinski's sign was positive for a few days. The temperature ranged between 98.6 and 99.6 F. On December 26, lumbar puncture was performed. The fluid was clear, under increased pressure, with negative Wassermann, Ross-Jones and colloidal gold tests. On Jan. 8, 1923, examination by one of us (P. B.) revealed all tendon reflexes to be present and the plantar reflexes normal. There was slight rigidity of the neck, but Kernig's sign was absent. The spinal fluid pressure was 24 mm. of mercury. It was free from globulin and cells, but there was a slight colloidal gold reaction in the higher dilutions (0000012111). There was temporary relief of headache after the puncture. Dr. E. B. Fowler found alternating convergent strabismus of about 15 degrees. Both disks were swollen, their borders blurred with striate appearance, cribriform not seen. For the next few weeks, the condition grew worse. Every few minutes, the child screamed with pain, and at times was in a stupor between pains. Vomiting persisted. A tentative diagnosis of brain tumor of unknown site was made, although the possibility of a postinfectious serous meningitis was considered.

On January 29, a right subtemporal decompressive operation was performed by Dr. Bevan. This relieved the headache considerably, but vomiting persisted, and after a few weeks, the patient passed into a stuporous state. A cerebral hernia gradually developed. On February 15, the temperature suddenly rose from 99 to 105.2 F., and remained high for a week. Subsequently, there were repeated similar periods of fever. Thus on March 24, the temperature was 106 F.; on March 31, 104.6 F. The swelling of the disk disappeared, and was replaced by the pearly white appearance of optic atrophy. The internal strabismus persisted. For months, the patient lay in complete stupor, recognizing no one and giving no expression of pain. The extremities became rigid, the feet in permanent equinovarus position. There was often difficulty in breathing, and from the beginning of March, the child was expected to die any day. She remained, however, in a state resembling "decerebrate rigidity," and was taken home, Aug. 25, 1923. After the last period of hyperpyrexia early in April, the temperature ranged between 100 and 102 F. The pulse rate was usually from 110 to 130, and the respirations from 20 to 40. The life of the child was apparently prolonged by occasional aspiration of cerebrospinal fluid from the hernia. The patient died on Jan. 19, 1924.

Anatomic Diagnosis.—The diagnosis was glioma of the pons; internal hydrocephalus; cerebral hernia, healed decompression wound.

The scalp on the right side bulged just above and behind the right ear in a place 5 cm. in diameter and 5 cm. high, due to cerebral protrusion. There was a surgical defect here in the cranial bones 4.5 cm. from front to back, 5 cm. from top to bottom, and about 3.5 cm. above the upper attachment of the right ear. The dura was adherent to the scalp tissues at the protrusion in many places The bulge was pedunculated, with the neck about 2 cm. in diameter. The calvarium separated easily from the dura and was of thin translucent bone. The convolutions of the upper surface of the brain were moderately flattened and the sulci narrow. There was no noteworthy change of the ventral surface of the pons or medulla. The markings were distinct and the blood vessels had thin walls. The under surface of the cerebellum was asymmetrical from a tumor in the left half close to the midline protruding from the surface about 3 cm. The markings of the under surface of the cerebellum were obliterated, and the tumor encroached onto the right half for about 1 cm. in the middle of the under surface. The cerebellum was larger than normal. When the pons and medulla were removed from the cerebellum in the usual way, light gray tissue occupied practically all of the surfaces made. The fourth ventricle was obliterated. A cross section through the pons at the level of the roots of the fourth cranial nerves was composed one half of apparently normal tissue and one half of tumor. The tumor had grown up into the cerebellum, and on the broadest surfaces that could be made by sectioning the cerebellum, it was 6.5 cm. wide and 4 cm. thick. In most places, the tumor in the cerebellum was sharply demarcated from the cerebellum by a membrane about 1 mm. thick. In a few places, there were narrow linear spaces with clear fluid between this membrane and the tumor tissue. When surfaces were made through the largest plane of the cerebellum and continued forward through the pons, there was a layer of pons tissue about 1 cm. wide at the ventral margin. The brachium pontis was narrowed to 3 or 4 mm., and the tumor was a mass 4.8 cm. high and 5.8 cm. wide. All trace of the fourth ventricle was lost, except for two cavities on the right side between the cerebellum and the tumor, that ended blindly. A coronal section through the hernia sac and tips of the temporal lobes showed that the lateral ventricles were greatly dilated, having here an average width of about 3 cm.; the one on the right side extended out to the hernia sac, and at its back end communicated with the hernia sac. The convolutions of these coronal surfaces were greatly flattened.

The trunk was not examined.

Histology.—The structure was uniform throughout. The glia cells were about equally round and oval. Cytoplasm was sparse. The cells were all separated from one another by from two to five glia fibers, and the latter formed a network with many spaces between. Fragmentation and a granular appearance was common in the glia fibers. There were a few small round spaces with cuboidal cells, one to three layers thick, forming their walls. The blood vessels were small and sparse and the walls thin. The tumor infiltrated the pons without sharp demarcation. There was little evidence of glia hypertrophy about the vessels. No blepharoblasts were demonstrated.

Case 3.—*History.*—A boy, aged 6, admitted to the Presbyterian Hospital on Aug. 1, 1923, had a history of mild diphtheria two years before and of measles one year before. He had been a habitual bed-wetter.

About July 10, he had been taken with a cold, with heavy mucous discharge from the nose. He choked easily, and his food had to be liquid or semiliquid. The speech became slow and nasal, with inability to whistle and to blow his nose.

Staggering gait had been noted a few weeks before the onset of the cold, and it afterward became more marked; he had repeatedly fallen. There was also incoordination of the hands, more of the left. Beginning two or three days after the onset of the cold, the boy had a tendency to retention of urine. The temperature had been 101 F. on the first day of the cold, but had been normal since then.

Examination on Admittance.—The patient was well nourished; speech was slightly impaired, but he still had some difficulty in swallowing solids. There was no stiffness of the neck and no Kernig sign. The pupils, ocular movements, and fundi were normal. There was no nystagmus. Hearing was good. There was no facial palsy. All tendon reflexes and the abdominal reflexes were normal, but positive Babinski and Oppenheim signs were obtained on both sides. These abnormal reflexes, together with slight paresis of the soft palate, constituted the only positive neurologic findings. Lumbar puncture yielded a clear fluid with negative Wassermann and globulin tests, negative colloidal gold test and no cells. The leukocyte count was 4,850 on August 1 and 5,950 on August 3. Otherwise the blood count was normal. The blood pressure was: systolic, 98; diastolic, 68. The temperature ranged between 98.6 and 99.8 F., the pulse rate between 56 and 100, the respirations between 20 and 26. At times the pulse was irregular, but there was no evidence of any heart lesion. On August 10, ankle clonus was obtained on both sides, and the Babinski sign remained.

The general condition remained good, and the next day the boy was taken to his home in another state. A tentative diagnosis of encephalitis of unknown origin was made.

On August 12, there was increased difficulty in speech and swallowing. Stiffness of the legs developed; the facial movements became impaired, and on August 24, both external recti became weak. Slight spasms with moaning and frothing at the mouth were observed, and the patient often choked, but was relieved when mucus was removed from the throat by a suction apparatus which was constantly kept at the bedside. Nasal feeding was instituted on August 18, and after that date, the patient never was known to swallow. The bladder frequently was distended, but the patient was able to void. On August 29, the temperature rose, and ranged from 100 to 103 F. The nasal discharge became foul, and contained encapsulated diplococci. The pulse rate ranged from 64 to 104. Vomiting was frequent, but the patient gave no expression of pain. When seen by one of us (P. B.) on August 31, the boy was in deep stupor. The pupils were small and equal; the eyegrounds were normal. The position of the eyes was normal, but the movements could not be tested. The tendon reflexes were rather brisk, the abdominal and cremasteric reflexes absent. A bilateral Babinski sign was present.

On September 1, diphtheria bacilli were reported to be present in the nasal secretion, and antitoxin was administered, following which the choking and pharyngeal secretions diminished. For a time, there were considerable cough and inspiratory stridor. The stupor continued. The patient never tried to talk, but at times would protrude the tongue. When again visited on September 27, the pupils and eyegrounds had remained normal. The eyes were moved upward and downward but not laterally. A bilateral Babinski sign was still obtained; the ankle reflexes were absent, the other tendon reflexes present. The abdominal and cremasteric reflexes were absent. There was some edema of the upper lip and across the nose.

On September 30, involuntary movements of the extremities were observed. The patient occasionally laughed and cried. Tonic spasms of the legs and grinding of the teeth occasionally occurred. The tendency to choking was absent for several weeks. When visited on November 7, the disks were still normal, and the other findings were practically as before. No new features developed, but the stupor and compete helplessness continued. The patient gradually failed, and died on Feb. 8, 1924.

Anatomic Diagnosis.—The diagnosis was glioma of the pons and cerebellum; internal hydrocephalus.

The calvarium was thin and indentations from the convolutions were distinct. The surface of the brain was smooth, and the sulci were obliterated. The ventral surface of the pons was irregular from gray flat nodules about 1 cm. in diameter and 1 to 3 mm. high, which obliterated the normal markings. The cerebellum was large, the outside unchanged, but both the ventral and dorsal surfaces of the pons were so changed by the tumor process that the normal landmarks were obliterated. The maximum width of the pons was 6 cm. In the cerebellum at its middle, extending from the pons back to within 2 cm. of the back margin of the cerebellum, there was a well circumscribed tumor about 7 cm. in diameter. Most of the inside was soft and mottled yellow and brown. In surfaces made by sectioning the pons through the midline, there was a gray, opaque tissue extending almost through and in some places through the ventral surface. Dorsally, the tumor extended into the cerebellum. About four fifths of the volume of the pons was made up of this gray tumor tissue. The fourth ventricle was obliterated.

The outside of the cerebrum was bloodless except for a few of the leptomeningeal veins of the upper surface, which were moderately engorged. The leptomeninges of the cerebrum everywhere were thin and transparent. The convolutions were flattened, and most of the sulci were obliterated. The lateral ventricles were large. Two centimeters behind the optic chiasma, each ventricle had a maximum width of about 2 cm. and a maximum height of 3.5 cm. Where the ventricles extended into the temporal lobes, they had a maximum width of 2 and 1 cm. and a maximum height of 1.5 and 2 cm. The left lateral ventricle extended forward to within 3.5 cm. of the frontal pole, the right to within about 3 cm. The lining of the lateral ventricles was smooth. The choroid plexuses were unchanged. Many surfaces made by sectioning the brain were pale. The cortex averaged about 4 to 5 mm. in thickness.

The trunk of his body was not examined.

Histology.—The tumor resembled that of Case 2 in most respects. Occasional "rosettes" and giant cells were present, but no spaces lined by cuboidal cells were found. There was the same lack of sharp separation between tumor and pons as existed in Case 2. Glia fibers predominated over cells.

CASE 4.—*Syndrome of left-sided pons lesion with rapid onset. Right hemiplegia and hemianesthesia and paralysis of left facial, motor fifth and conjugate eye movements.*

History.—A salesman, aged 38, was admitted to the hospital on July 12, 1924, with a history kindly furnished by Dr. A. G. Asher of Ft. Dodge, Iowa. For several months, the patient had been getting tired and drowsy more easily, but this was attributed to unusually heavy work. About May 1, he began to see double on looking to the left and to have attacks of transient faintness. On May 12, it was noted that the diplopia was due to weakness of the left abducens and that slight nystagmus was present. Vision and hearing were good, and the

knee reflexes were increased. Gait and all movements, except of the eye, were normal. The blood pressure was: systolic 120; diastolic, 80. The blood Wassermann test was negative (had also been so eight months previously). The spinal fluid was under normal pressure; there were 6 cells to the cubic millimeter; the globulin test was negative, and the Wassermann test was reported positive (+ + +) at one laboratory and negative at another. After two days, the patient for the first time had severe headache, vomiting and slight stiffness of the neck. He had to stay in bed for a week, and then improved sufficiently to go on a 200 mile automobile trip. On the way home, about June 28, 1924, he again began to vomit; at the same time he developed weakness and awkwardness, first of the right leg and then of the right arm. After a few days, there appeared paralysis of the left side of the face, deafness in the left ear and difficulty in swallowing, but there was no more headache and no vertigo. Loss of sensation of the right side of the body except the face developed about July 5.

Examination.—On admittance to the hospital on July 12, all left facial movements were weak. Nystagmus and diplopia were present when the patient looked to the right. Neither eye could be moved to the left of the median line. Rotary nystagmus and diplopia appeared when he looked upward. The right pupil reacted fairly well to light; the left, not at all; both reacted in accommodation. There was no hemianopsia. Ophthalmoscopic examination was negative. Hearing in the left ear was impaired. The left masseter muscle was paralyzed. The tongue was not atrophic and was protruded straight. The left palate was rather weak. Recumbent, he could raise his head, and when he did this, the right sternomastoid contracted, but he could not shrug the right shoulder nor move any muscle in the right arm or fingers except flex the elbow a little by means of the supinator longus. The right side of the chest was moved less than the left in respiration, and thoracic breathing was stronger than diaphragmatic. He could raise the right foot about 10 inches from the bed. The ankle movements were weak, those at the knee and hip slightly better. The strength on the left side was good except in the face, as stated. The left plantar reflex was normal, while there was no response on the right. Abdominal reflexes were not obtained. Tendon reflexes were normal on the left, slightly increased on the right. Tactile sense was impaired on the entire right side, while pain and temperature sense were preserved in the face but lost on the rest of the right side. The sense of position was impaired in the right hand, and vibration sense was impaired in the right extremities. There was some difficulty both in articulation and swallowing.

Course of Illness.—Spinal puncture on July 13 yielded a clear fluid, and all of the usual tests were negative, as was the blood Wassermann test. Hiccup started four hours after the puncture, was very troublesome for four or five days and recurred at varying intervals until July 25. On July 18, the temperature rose, and signs of bronchopneumonia appeared, but disappeared again on July 23, when the patient began to feel better in every way. On July 25, it was noted that the left side of the forehead was almost dry, while the right side perspired freely. Both eyes remained to the right of the median line, could not be moved to the left, and only about 20 degrees to the right. The downward movement was good, the upward movement a little restricted. The patient complained of left frontal headache on that day, and two days later this was more severe. On July 27 he grew worse, breathing became difficult and projectile vomiting occurred. On July 29, the temperature rose rapidly from 99 to 103.6 F., and the patient died in the evening.

The clinical diagnosis was definitely made as far as a lesion on the left side of the pons was concerned, but there was some doubt until the last as to whether it was inflammatory or neoplastic.

Anatomic Diagnosis.—The diagnosis was: glioma of the pons; internal hydrocephalus; thrombosis of the left sigmoid sinus; marked emaciation; hypostatic bronchopneumonia; marked purulent bronchitis.

The dura was thin and moderately tense all over the top of the brain. The calvarium was easily removed from the dura. In the superior longitudinal sinus,

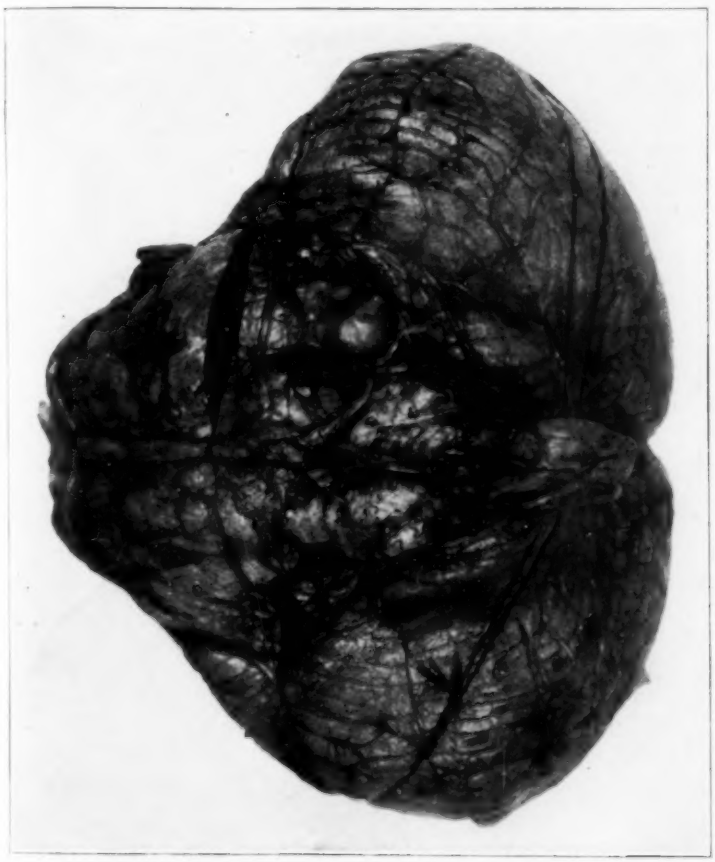

Fig. 2 (Case 4).—Under surface of the pons, medulla and cerebellum, showing the enlargement of the right half of the pons and partial obliteration of the junction of the pons and medulla on the right side by a small protrusion.

there was a loose, dark red, smooth clot. The leptomeningeal veins and small radicles were markedly distended on the right side and only moderately on the left. The cerebral convolutions were flat. The sulci were wide, and the leptomeninges were thin. The brain was soft. The maximum width of the pons was 5.5 cm., 2.5 of which were to the right and 3 to the left of the basilar artery. The prominence of the left side was chiefly of the inferior half, and extended toward the cerebellum. On the left side at the junction of the pons

and medulla, there was an irregular oval mass 1.5 cm. from front to back, 1 cm. across and about 6 or 7 mm. high. The upper end of the medulla was 2.4 cm. wide, its right half was 1.5 cm. wide, and the junction between the pons and medulla was almost obliterated. The pons was light gray. Some of the larger veins about the pons were engorged with blood. The left sigmoid sinus was

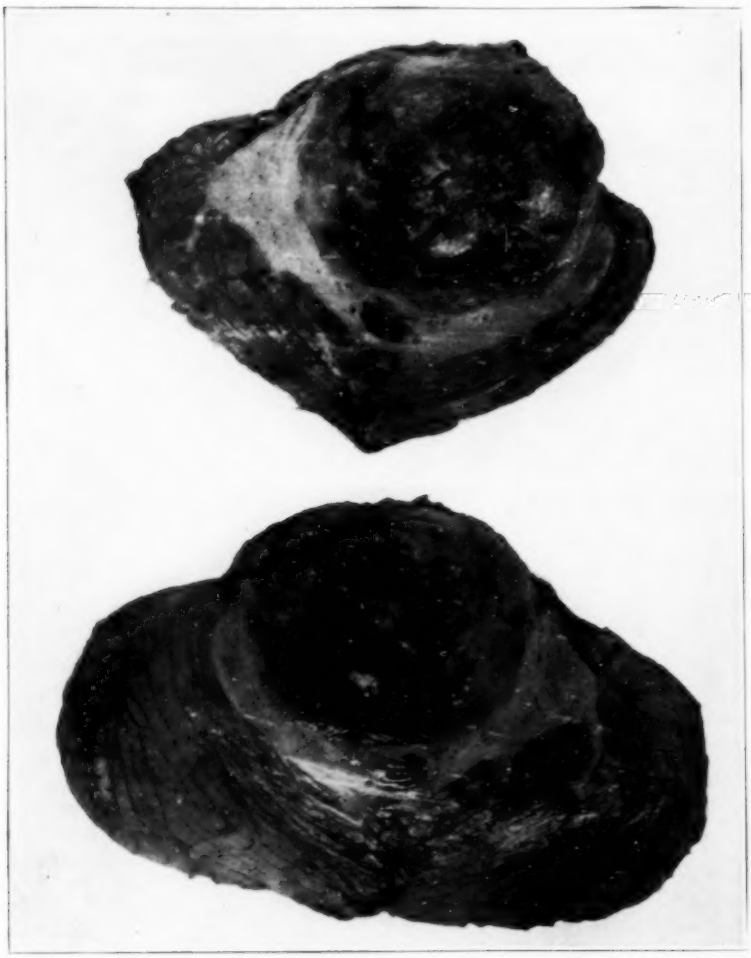

Fig. 3 (Case 4).—A cross-section of the pons and cerebellum showing the extent of the tumor where it was largest.

occluded by a gray and red mottled clot extending 1 cm. to the right of the midline in the right lateral sinus. This clot was oldest close to the jugular vein. There was no gross sign of inflammation of either middle ear. The anterior and posterior clinoid processes were rounded and normally smooth. The pituitary gland was not enlarged. The lining of the frontal, ethmoid and sphenoid sinuses was smooth.

The brain was hardened in liquor formaledhydi. The maximum width of the pons was 5.5 cm., of which 3 cm. were to the left of the midline. The ventral surface of the left was more prominent by 2 or 3 mm. than the right side. The junction between the pons and medulla on the left side was obliterated for 2 cm. Surfaces made by sectioning the pons through its widest part were made up of a tumor 3.8 cm. wide and 3.2 cm. high, the periphery 1 to 7 mm. wide, light gray, opaque and slightly firmer than the brain tissue. The center of the tumor was made up of a soft and semifluid gray-yellow to gray-green tissue. At the dorsal part of the tumor, a soft tissue came within 1 mm. of the floor of the fourth ventricle, which was here flattened out, forming a slightly curved slit 2 cm. long. Most of the pons tissue was on the right side and ventral part. Surfaces made by sectioning the pons at the level of the exit of the fifth cranial nerves were 5 cm. wide, the right side 3.5 cm. high, the left 4.1 cm.; the left side 3 cm. wide and the right 2 cm. The most superior level of the tumor tissue was in the coronal section through the pons at the level of the inferior end of the aqueduct of Sylvius. Here there was a green region to the left and beneath the floor of the aqueduct and the pons was deformed, the left side greatly enlarged, because of the presence in the upper left quarter of hard gray tissues. Grossly, at the level of the fifth cranial nerve, the tumor did not extend into the brachium pontis or conjunctivum. Gross evidence of pyramidal fibers and cross fibers were limited to the ventral part of the pons on the right side. At the level of the junction of the pons and medulla, the floor of the fourth ventricle slanted upward to the left, and the tumor had here invaded the brachium pontis, pushing it toward the left. Surfaces made by sectioning through the upper end of the spinal cord were asymmetrical, uniformly light gray-yellow, the left half 2 cm. high, the right 2.5 cm., the left 1.5 cm. wide and the right 0.8 cm. The cerebrum was symmetrical, the convolutions flattened, and the sulci obliterated. The lateral ventricles were widened and elongated so that in the middle of the brain at the level of the optic chiasma, they were 4 cm. wide. At the level of the tips of the temporal lobes, they were from 5 to 6 cm. wide. The third ventricle was greatly dilated, so that it had a maximum width of 11 mm. and a maximum height of 24 mm. Five centimeters from the occipital poles, the ventricles were 2.4 by 1.3 cm. each. From the posterior ends, the lateral ventricles extended forward into the temporal lobes as far forward as the level of the optic chiasma.

Histology.—The cellular elements were prominent. The nuclei varied from those about the size of a round cell to almost ten times as large. Most of the nuclei were vesicular; some stained heavily with hematoxylin. Multinucleated cells were common. The glia fibers were sparse except about some of the blood vessels. Most of the blood vessels were small, and most had walls consisting of a single layer of endothelial cells.

Diagnosis.—Glioma.

DISCUSSION

DR. GEORGE W. HALL: May I ask Dr. Bassoe whether the findings in the optic disks were not misleading in two of the cases? In these cases internal hydrocephalus was present, and yet the disks were normal.

DR. PETER BASSOE: Yes, that was what made us persist so long in the diagnosis of encephalitis.

DR. G. B. HASSIN: How would Dr. Bassoe explain that he obtained spinal fluid by lumbar puncture, in his first case, in which the fourth ventricle was filled with a tumor mass? The fluid originating, according to current teachings,

from the choroid plexuses of the lateral ventricles, evidently could not escape through the foramina of Magendie and Luschka causing an internal hydrocephalus. The condition was analogous to that experimentally produced by Weed, who blocked the escape of the ventricular fluid by obstructing the Sylvian aqueduct. He does not say whether he could obtain fluid by a spinal puncture after obstructing the aqueduct in animals. Dr. Bassoe could in his case, which shows that the cerebrospinal fluid does not originate from the choroid plexuses but elsewhere.

Dr. Julius Grinker: Dr. Bassoe's second and third patients were apathetic, drowsy and practically lifeless for days or months. This symptom is found not only in epidemic encephalitis, but in large cerebral tumors. A recent patient with a frontal lobe tumor presented the epidemic encephalitis syndrome for months; a mere vegetating automaton. She ate only when food was placed in her mouth and spoke in monosyllables. I should like to know in how many of the cases the lesion was diagnosed.

Dr. Albert B. Yudelson: Was taste tested in the fourth case, and was progression and regression of involvement of this sense noted?

Dr. Peter Bassoe: The correct diagnosis was made in only the first case after making a ventriculogram. In the others, no correct localizing diagnosis was made except in the fourth case, but here we did not know whether or not it was a tumor. I performed a spinal puncture in the case mentioned by Dr. Hassin, and found the fluid to be under a pressure of 17 mm. of mercury. At the next puncture, it was under a pressure of 22 mm. of mercury; so the fluid did get into the spinal canal. The tumor did not entirely fill the fourth ventricle, but it did project into the ventricle which was dilated. Then, too, such tumors grow rapidly, so that it was not nearly so large when the punctures were made, and certainly a channel existed for the fluid to escape through.

We did not have an opportunity of testing accurately the sensation of taste. All of these patients were extremely sick, and could not be examined easily. Vestibular tests were made in the first case, but had to be stopped because of the intense reaction produced.

The condition of the optic disks was certainly misleading. The absence of choked disks does not rule out a tumor, even in the posterior fossa. This is particularly true in children in whom the sutures may be separated.

Abstracts from Current Literature

Relation of Blood Sugar to Spinal Fluid Sugar and Diagnostic Value of Spinal Fluid Sugar Determinations. F. G. Dietel, Ztschr. f. d. ges. neurol. u. Psychiat. **95**:563 (March) 1925.

The diagnostic value of spinal fluid sugar determinations has been the subject of numerous investigations. That a decrease in the spinal fluid sugar is a valuable diagnostic aid is pretty well accepted, but no such unanimity is found with regard to an increased spinal fluid sugar (hyperglycorrhachia). The present investigation is concerned with the following problems: (1) the relaton of the blood sugar to the spinal fluid sugar, (2) possibility of a hyperglycorrhachia without a hyperglycemia, (3) diagnostic value of increases in the spinal fluid sugar. The method used in the sugar determinations was the Folin-Wu method. The normal blood sugar was taken as from 100 to 130 mg. per cent. with an average of 115 mg. per cent. The normal spinal fluid sugar was regarded as 50.75 mg. per cent., with an average of 64.2 mg. per cent., and the relation of the blood sugar to the spinal fluid sugar was roughly 2:1. Other investigators found similar values for the normal spinal fluid sugar; e. g., Eskuchen, 45 to 60 mg. per cent., Borberg (1916) 50 to 75 mg. per cent., Steiner (1923) 55 to 80 mg. per cent., Scham and Nixon (1921) 45 to 95 mg. per cent., and Mestrezat (1922) 55 to 65 mg. per cent.

The literature contains only a few contributions to the relation of the blood sugar and the spinal fluid sugar. Wittgenstein found the spinal fluid sugar to be from 50 to 80 per cent. of the blood sugar, and Scham and Nixon found it to average about 56.2 per cent. of the blood sugar. That the sugar content of the spinal fluid is less than that of the blood is generally agreed, but in what proportion is not a matter of general agreement, nor will it be until the nature and source of the sugar is more accurately determined. Accepting the fact that the fluid sugar is less than that of the blood sugar, two views prevail as to its mechanism. Polonowski and Duhot found that the spinal fluid sugar varies concomitantly with the blood sugar, even though in small degree. They proved this both by the experimental production of a hyperglycemia by means of epinephrin, and by feeding sugar by mouth. They concluded that it was impossible to determine accurately the normal values of the spinal fluid sugar, however, because of great individual variations, and because the fluid sugar is influenced by extraneous factors such as the sugar content of the alimentary canal. For this reason they doubted the value of a hyperglycorrhachia unless accompanied by a blood sugar determination. Mestrezat, on the other hand, found a normal value of the spinal fluid sugar (55-65 mg. per cent.), and also found that the relation between the blood and fluid sugars was variable. Most investigators agree with Mestrezat so far as normal values are concerned. But the dependence of the spinal fluid sugar on the blood sugar is by no means clear, especially in the physiologic variations. Wittgenstein found no increase in the fluid sugar with an alimentary glycosuria, but he found a definite hyperglycorrhachia in diabetes. Strong assumes that a hyperglycemia from any cause is accompanied by hyperglycorrhachia. Kabler found this to be true in diabetes, uremia and apoplexy. Schloss and Schroeder and Scham and Nixon found that the spinal fluid sugar varies with the blood sugar. The author attempted to determine how far the spinal fluid sugar

is influenced by an alimentary glycocemia, and also to determine the relation between blood and spinal fluid sugars by the intravenous injection of dextrose, thus producing an experimental glycocemia. He found in every case that an increase in the blood sugar was followed by an increase in the spinal fluid sugar, even though the latter was slight. The fluid sugar reached the maximum thirty minutes after intravenous injection and sixty minutes after oral administration. The blood sugar maximum varies after intravenous injection of dextrose, but the initial level is reached about two hours after injection. This agrees with the findings of Foster, Gray and Jorgensen, and the same is true after the ingestion of sugar by mouth. The normal relationship of the blood and spinal fluid sugar is never exceeded or diminished. The possibility of a psychic cause for the increase in the fluid sugar is not conceded by the author because of the delayed rise in the sugar level. He agrees, however, that there are sources of error in determining a hyperglycorrhachia which cannot be overlooked. These are: 1. There are people with a normally high blood sugar (John), and these people have a correspondingly high spinal fluid sugar. 2. Werrien and Pierron found a hyperglycemia in seven out of sixteen cases after lumbar puncture, due to excitement and anxiety. 3. Eskuchen agrees that hyperglycemia may follow a lumbar puncture by alteration of the central sugar regulating mechanism. 4. Not only lumbar puncture, but often irritative conditions may cause a hyperglycemia in the same way. In three cases with an absolute, long standing hyperglycemia as in diabetes a hyperglycorrhachia was found in three determinations, and a normal sugar once. In six cases of fever, hyperglycorrhachia occurred six times. So that the author concludes that in a long continued hyperglycemia the spinal fluid sugar increases.

In summarizing his own investigations, the author states that (1) there is a direct dependence of the spinal fluid sugar level on the blood sugar level since a hyperglycemia is regularly followed by a hyperglycorrhachia, but (2) that in the cases with a normal blood sugar and a hyperglycorrhachia the reason for the increase in the spinal fluid sugar cannot be sought in alimentary causes. He lays great stress on the simultaneous blood sugar determination in making spinal fluid sugar determinations. In thirty-six cases with a hyperglycemia he found a normal fluid sugar in 61 per cent., a hyperglycorrhachia in 16.7 per cent., and a hypoglycorrhachia in 22.2 per cent. In another series of cases, however, he found a definite and consistent hyperglycorrhachia with normal blood sugar. He quotes Eskuchen as stating that a hyperglycorrhachia may be produced without hyperglycemia, i. e., primarily by various factors such as increase in pressure or by toxic or inflammatory causes. Eskuchen considers the following possibilities in hyperglycorrhachia: (1) primary hyperglycemia: causing a secondary physiologic hyperglycorrhachia; (2) injury to the filtering membranes: secondary pathologic hyperglycorrhachia due to toxic, inflammatory, congestive, or functional causes; (3) irritation of the sugar-regulating center. (*a*) Local: toxic, inflammatory, mechanical. (*b*) General: through pressure increase. To continue with the author's experiments, however, of eight cases with a decreased blood sugar, the spinal fluid sugar was normal in seven cases. The author draws the following conclusions: 1. A hyperglycorrhachia occurs without a hyperglycemia, though the latter usually is accompanied by the former. 2. So far as alimentary influence can be ruled out: (*a*) An increase or decrease in the spinal fluid sugar may be looked on as pathologic if the blood sugar is normal and if the fluid sugar is absolutely increased or decreased. (*b*) A hyperglycorrhachia need never be considered as pathologic if the blood sugar is below normal. (*c*) A decrease in the spinal

fluid sugar need never be considered as pathologic if the blood sugar is increased but the spinal fluid sugar is within normal limits.

It is generally recognized that an arterial hypertension frequently causes a hyperglycemia, which if it be of sufficiently long standing causes in turn a hyperglycorrhachia. Eskuchen found a hyperglycemia in 50 per cent. of his cases of hypertension, and with this a frequent hyperglycorrhachia. Kahler stated that the blood sugar is increased in cases of hypertension only in the presence of certain complications, such as apoplexy, uremia and pancreatic sclerosis. He constantly found a hyperglycorrhachia under such conditions. He conceded the possibility of a hyperglycorrhachia without a hyperglycemia in cases of essential hypertension, having found this true in 50 per cent. of such cases. In fourteen cases of hypertension investigated by the author, the blood sugar was increased in nine, or 61 per cent., and the spinal fluid sugar in two, or 22 per cent. In four cases the fluid sugar was increased without a concomitant hyperglycemia. In thirty-five cases with increased spinal fluid pressure, the spinal fluid sugar was increased in sixteen cases, or in 46 per cent.

In his investigation of the spinal fluid sugar in various diseases the author found a hyperglycorrhachia in serous meningitis, cerebrospinal syphilis, brain tumor, multiple sclerosis, syringomyelia, neurasthenia, hysteria and diabetes. The sugar was decreased in purulent or tuberculous meningitis. He states that the value of the decreased sugar in tuberculous and purulent meningitis in differentiating these conditions from similar disease pictures is undeniable. A hyperglycorrhachia must be used more carefully as a diagnostic means, however. It is of distinct value in epidemic encephalitis. Certain authors have considered it of value in differentiating hysteria from epilepsy. Wittgenstein, for example, found a hyperglycorrhachia in 100 per cent. of epileptic patients, but never in hysteria; Hess and Pötzl corroborate these findings. The author finds, however, that hysteria may produce a hyperglycorrhachia, and he doubts the value of this finding.

In thirty-nine cases in which lumbar puncture was performed, a simultaneous cistern puncture was performed with the following results: (1) In twenty-eight cases, or 72 per cent., the cistern sugar content was higher than in the lumbar fluid; (2) in three cases, or 8 per cent., it was the same; (3) in eight cases, or 20 per cent., it was lower than in the lumbar fluid. Hence the cistern fluid has a higher sugar content in the majority of cases than does the lumbar fluid.

In three cases simultaneous ventricular, cistern and lumbar puncture was performed. In all three cases the ventricular fluid showed a higher sugar content than the cistern fluid, which in turn showed a higher content than the lumbar fluid.

ALPERS, Philadelphia.

NYSTAGMUS: NEURO-OTOLOGIC STUDIES CONCERNING ITS SEAT OF ORIGIN. I. LEON MYERS, Am. J. M. Sc. **169**:742 (May) 1925.

In the biphasic movements of the eye known as nystagmus the first phase consists of the deviation of the eyes from the position of rest and fixation and the second phase the returning to or near the original position. The movement in the first phase is known as the slow component, the second phase the quick component. The type of nystagmus is named for the quick component. The phenomenon, if the nystagmus seen in degenerative disease of the choroid and retina is not considered, is the motor manifestation of an

excitatory process in the vestibular system, either in the labyrinth along the course of the vestibular nerve as far up as its termination in Deiters' nucleus and nucleus of Bechterew in the pons, or in the nuclei tecti of the cerebellum. Whether the second afferent neuron is also associated with nystagmus is not known. Experimental evidence tends to show that excitation of these lower tracts produces only conjugate deviation of the eyes and its allied phenomena. The excitation may be produced artificially in the Bárány tests by irritation of the labyrinth by disease or by unantagonized activity of one intact vestibular system when the other has been destroyed. The nystagmus may not always be biphasic. In lower vertebrates it is limited to a slow deviation of the eyes with no tendency to a return reflex. A reaction is also observed in man under a marked degree of narcosis. The slow component, therefore, is probably the more primitive and elementary motor reaction, and consequently the more resistant of the two, having its seat of origin in the lower motor nuclei — the pons and midbrain. The seat of origin of the quick component has not yet been determined. Bárány placed it in the cerebellum; Bartels in the cerebrum; and Bauer and Leidler, in experimental studies, found it present when the cerebrum and optic thalami were destroyed. Wilson and Pike found that the quick phase was abolished by the removal of the cerebrum and the optic thalami. Ivy thought it was determined entirely by centers below the thalamus.

To determine the seat of origin of the quick component, the author studied sixteen cases of hemiplegia with conjugate deviation of the eyes for a variable time following the stroke. Experimental evidence shows that laterogyric action of the head and eyes may be brought about by the stimulation of one of two regions in each hemisphere, namely, the motor zone, or, more specifically in the middle and inferior frontal convolutions in the frontal lobe; and another area in the sensory zone, or, more specifically, in the angular gyrus of the parietal lobe. The abolition of this function in one hemisphere allows the laterogyric action of the other hemisphere to come into play unantagonized, thus rotating the head and eyes toward the side of the lesion. This condition is pronounced for a day or two following the stroke, then becomes progressively attenuated, so that at the end of a week or ten days it is hardly noticeable. Labyrinthine stimulation during this period of conjugate deviation of the eyes should not cause a rapid phase to the side opposite to the lesion whenever the stimulation is such as would produce normally a nystagmus to that side if the rapid phase had its origin in the motor area of the cerebrum, but should produce a normal reaction if both phases originated in the midbrain and pons and were independent of the cerebrum. Four cases were then reported to illustrate this study.

The first patient had right-sided hemiplegia with both sensory and motor aphasia with conjugate deviation of the eyes to the left. She was able to move the eyes now and then spontaneously to the right, was fully conscious, but could not utter a word. On douching the right ear with water at 68 F., with the head 60 degrees back, the eyes, after twenty seconds, were drawn to the right, and there occurred a horizontal nystagmus to the left. It was normal in rhythm and amplitude. On douching the left ear, the eyes, after twenty seconds, were drawn to the extreme left angle where they manifested a slight nystagmus to the right; this ceased after a few moments. In spite of the prolonged douching, there was no further disturbance in the eye. The following day, when the patient was unconscious no vestibular response was obtained by irrigating either ear; when the patient was conscious, the slow component only was obtained on irrigating the ear on the side of the lesion, but a more or

less normal nystagmus occurred on irrigating the ear on the opposite side, i. e., the side of the paralysis. It would seem possible to conclude, therefore, that a lesion of the lateral gyric center, or its conducting tracts in the internal capsule on one side, abolishes the quick component of nystagmus to the other side, but does not affect the slow component. The author, however, thinks that the slow component is modified in extent.

Necropsy showed a thrombosis of the left middle cerebral artery with softening of almost the whole left cerebral hemisphere with practically no involvement of the right hemisphere, cerebellum, pons and medulla.

In Case 2 there was a left-sided hemiplegia of the capsular type, with slight involvement also of the right side, loss of the rapid phase on irrigating the right ear with cold water, with a tendency toward an atypical response on irrigating the left ear. However, the reaction obtained after irrigating the left ear was almost normal. The patient was unconscious during the examination.

The third patient had right-sided hemiplegia with Broca's aphasia and conjugate deviation to the left. There were no sensory changes, and the patient was fully conscious. On irrigating the right ear, the slow deviation reached only the midline, where the rapid phase began pulling the eyes into the left canthus. On irrigating the right ear, there was an increase in the previous conjugate deviations of the eyes to the left. During the latter irrigation, there was a tendency of the eyes to become dissociated in their direction of fixation, the left eye remaining fixed in its direction to the left, while the right eye moved more to the right and remained in the midline, suggesting that in laterogyric action of the eyes, each hemisphere enervates more powerfully the contralateral eye. In several cases, as late as three months after their injury, it was noted that although all signs of an apoplectic stroke had disappeared, the labyrinth tests were still affected.

Case 4 was that of a taboparetic patient who had chronic convulsions of the right side with head and eyes turned to the right. Cold caloric tests of the right ear accentuated deviation of the eyes to the right, but with no rapid movement toward the left. Stimulation of the left ear gave a biphasic reaction toward the right but with a definitely increased amplitude. These tests were made while the patient was in coma; while later, after he had recovered from the coma, the reactions obtained from the left ear were much greater than those obtained from the right.

In conclusion: First, in cerebral hemiplegia of vascular origin during the period of conjugate deviation of the eyes to the side of the lesion, it appears to be impossible to evoke nystagmus to the side opposite to the lesion, but a persisting and infrequently intensified conjugate deviation is produced toward the side of the lesion. Second, abnormal results may be obtained from labyrinth stimulation in patients with a hemiplegia months after the occurrence of the injury. Third, the motor impulse for the rapid phase of the nystagmus originates in the cerebrum, most probably in the laterogyric center of the eyes, which is situated, in accordance with the researches of Blevor and Horsley, in the middle and inferior frontal convolutions, although the corpus striatum undoubtedly plays a part in the production of this phenomenon. Four, the motor impulse for the slow phase of nystagmus originates in the nuclei of the eye muscles in the midbrain and pons, but is influenced to some extent by a cerebral activity.

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DIAGNOSIS AND TREATMENT OF SCIATICA. PAUL SCHUSTER, Klin. Wchnschr. **4**:316 (Feb.) 1925.

Many cases of pain in the hips and limbs are diagnosed as sciatica when, as a matter of fact, but few cases are true neuralgia of the sciatic nerve. A diagnosis of sciatica should be made in cases in which the pain is confined to the area of ramification of the sciatic nerve, its roots or one of its branches. The objective findings apparently are negative, especially if there is no foundation for the existence of an affection of the joints, the bones or soft parts. We speak of a neuralgia only when the changes in the nervous substrata do not present marked objective clinical signs, and the same may be said of sciatica.

The chief symptom of sciatica is pain which localizes in the area of the sciatic nerve and its branches and the fibers originating from the sciatic plexus, especially the cutaneous femoris posterior. The pain accordingly is in the gluteal region, and from there descends on the flexor surface of the thigh to the flexor and outer side of the leg below the knee and down to the sole or dorsum of the foot. Frequently the pain is confined to but a portion of this area, and may affect only the thigh or lower limb. The pain is not of a paroxysmal shooting character, but is more constant—diminishing and increasing. It is described as a pulling, gnawing, burning penetration of the muscle masses. Usually it is not aggravated by motion, but, on the contrary, is often less bearable when the patient is at rest. The pain is not maximal. If a patient lies abed and screams and moans, something other than neuralgia may be looked for, as a tumor of the spine, pelvis, etc. Sciatica differs from other organic leg pains in that it is not continuous for days or weeks, but tends to remission. Although general motion does not produce or call forth the pain, certain movements do; for instance, when the patient bends down from the hips, the nerve and muscles of the flexor side of the thigh are taxed and the pain appears.

The Lasègue sign is a constant symptom in sciatica, though it must by no means be looked on as pathognomonic of this disease. Much less constant are the so-called pressure points at the exit of the nerve in the buttocks, in the middle of the flexor side of the thigh and in the middle of the popliteal space. Frequently pressure points are overlooked, and the pressure sensibility is not always confined to typical points. The painful limb is not sensitive to gentle and careful movement, though it may be sensitive to cold and to psychic excitement. It is noteworthy that the pain increases during the night.

True sciatica is always one-sided. Complaint of bilateral pain suggests trouble in the spine or cauda equina. Some striking characteristics are scoliosis, sometimes on the painful side, sometimes on the opposite and sometimes alternating from one side to the other. Twisting of the vertebral column seems to alleviate the pain reflexly in some cases; then again there may be definite nerve root irritation. An outstanding characteristic of sciatica is the rigidity of the spinal column, but this stiffness alone would not warrant ruling out a possible organic disease of the spine.

In true sciatica there is but slight change in faradic response; retardation of galvanic response is suggestive of something else. Likewise there must be no gross change in the tendon reflexes.

Pain in the hip region is a common symptom in many diseases, and must be considered in the differential diagnosis. There may be a picture of real sciatica which is purely functional; neurasthenic persons and occasionally epileptic patients complain of such pains here and elsewhere, which disappear in a day or two. Varicose veins and hemorrhoids, flat foot, genu valgum and other abnormalities in the lower extremities which may be responsible for muscular overexertion sometimes give rise to similar symptoms. Pressure

sensibility will aid greatly in correct diagnosis, but pressure sensibility of the muscles due to myalgia rather than neuralgia must be differentiated.

The diagnosis of sciatica is not easy. The safest method is to rule out those cases in which there is some organic process causing the pain; first and foremost among these are tuberculosis or tumorous affection of the lower column, chronic inflammation of the vertebral joints, traumatic bone fissures, and, rarely, osteomyelitic processes. In sacro-iliac disturbances the seat of pain does not correspond to the course of the sciatic nerve, and pressure sensibility confines itself to the joint and vicinity. Joint diseases are betrayed by jolting or hitting against the sacrum or pulling of the feet. Exudates of the pelvis, tumors of the rectum, bladder, prostate, ovaries or uterus affect the sciatic nerve or its roots through pressure. Toxemia from diabetes, nephritis, gout, etc., may give rise to symptoms of sciatica. Organic affections of the lower portion of the spine, the cauda equina and meninges and syphilis may also cause symptoms. Symptoms arising from the foregoing causes, however, appear in a different degree than those arising from true sciatica. Pain is complained of in intermittent claudication, but, since in this condition symptoms appear only on walking, the arteries of the foot do not pulsate, and as there are no Lasèque sign and pressure points, there should be no difficulty in making a diagnosis.

The treatment of true sciatica is described. Only in cases in which pain is extremely severe is it practicable to keep the patient in bed. Hot applications, thermal baths, hot packs, the application of hot sand bags for hours at a time are recommended, and the patient should be so lodged for the night that his pelvis rests on one of these half filled pillows. Then dry cupping glasses, steam douches, rubbing and other methods that produce skin hyperemia are recommended, and if there is still no relief, diathermy is resorted to. Of all applications, diathermy is the most promising. Hot baths followed by damp packs, electric sweat baths, etc., may be tried, but frequently do not help, and sometimes aggravate the pain. The stage of the disease process largely determines the effect which the foregoing methods, as well as massage, may have. In early cases with severe pain, the author has not seen good results from massage.

Stretching the nerve is not recommended in beginning sciatica. Perhaps some results may be obtained from treatment with constant electric current 5-1-MA stable electrodes. Recently it has seemed that high frequency current or roentgen-ray treatment of the nerve roots combined with diathermy has been beneficial.

The best results, no doubt, have been obtained from injections of substances which are not likely to do harm; therefore alcohol must be avoided. The author has had good results with an 0.5 solution of procain and similar preparations. As it seems essential to strongly infiltrate the nerve and vicinity, it is necessary to have a sufficient amount of either betaeucainal hydrochloridums or procain carefully measured. As it is not always easy to reach the nerve for one who is inexperienced, the simple injection of the paraneural sheath is suggested, or injection into the sacral canal according to the method of Cathelin. Up to 100 c.c. of a 0.5 to 1 per cent. procain solution may be injected (the skin at no time must show infiltration). Quick results are usually obtained. More recently the injection of albumin and similar material has been employed in the treatment of sciatica. This, of course, would be resorted to only in case of failure with the injections named above.

In spite of the good results with the injection method, one cannot get away from medicinal measures. It may be necessary to employ salicylate prepara-

tions, especially during the early stages. Attention must be given to the free evacuation of the bowels. In every case the physician should be prepared to try a number of methods of treatment, as there are few diseases in which it is necessary to change the treatment so frequently as in sciatica.

MOERSCH, Rochester, Minn.

INTERCHANGE BETWEEN BLOOD AND SPINAL FLUID IN SYPHILITIC AND NON-SYPHILITIC PERSONS. SECOND CONTRIBUTION. W. SCHÖNFELD and W. LEIPOLD, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:473 (March) 1925.

This is the second contribution by these authors on this important subject. The research is divided into two portions, one with fluorescent substances such as uranin and esculin, and the other with the common dye phenolsulphonephthalein. Eleven patients were given from 1 to 5 c.c. of a 1 per cent. uranin solution, and the spinal fluid was withdrawn at intervals up to twenty-eight hours, but no uranin was visible in the spinal fluid to the naked eye. Thirteen patients were given 10 c.c. of a 1 per cent. uranin solution, and the spinal fluid was withdrawn at intervals of one and one-half to thirty minutes and after two, three, four, eleven and twenty-three hours, but in all the fluid was clear. With a polariscope, however, a slight clear greenish fluorescence could be seen in the fluid from one and one-half minutes to eleven hours after intravenous injection. Four fluids examined at thirty minute intervals from patients who had been given a 2 per cent. solution showed clear to the naked eye. With the polariscope, however, they showed a fluorescence. Forty-nine experiments with a 3 per cent. uranin solution showed the fluid to be uranin positive up to eighteen hours after injection; after twenty-two hours it was doubtful, and after twenty-nine, forty-eight and seventy-two hours it was uranin negative. Experiments with 4 per cent., 5 per cent. and 8 per cent. uranin solutions gave similar results. The authors conclude therefore that under normal conditions uranin passes into the spinal fluid, the amount probably depending on the amount and concentration of the dye introduced. In an attempt to quantitate the uranin which passed into the spinal fluid, the authors found that there was great individual variation, and that there was no outspoken impermeability to uranin.

Experiments with esculin, another fluorescent substance, demonstrated the presence of the dye in the spinal fluid two, seven, fifteen and twenty minutes after its intravenous injection. In one case it was demonstrated two and one-half hours after injection, but in the same case it had disappeared after five hours. With the polariscope the dye was demonstrable in every case twelve hours after injection.

The conclusions drawn are that fluorescent dyestuffs such as uranin and esculin pass in slight amounts into the spinal fluid as readily diffusible substances under normal conditions even if the blood is not overconcentrated with it. The dyestuffs are bound up with the albumin of the blood, and it is only the unbound dyestuffs which pass into the spinal fluid. The building power of the blood colloids for these substances, moreover, seems to be limited. In patients with changes in the cellular and albumin content of the spinal fluid the substances pass over in increased quantities.

The investigations with phenolsulphonephthalein were carried out on fifty-nine patients in whom seventy experiments were performed. In these cases lumbar puncture was performed, the bladder emptied, and a catheter kept in place. Urine was allowed to drop into a container of tenth normal sodium

hydroxid, and the first appearance of a discoloration in the alkali was taken as the first appearance of the dye in the urine. In this way it was found that on intraspinal injection of 3 mg. of phenolphthalein after lumbar drainage the dye appeared in the urine in from six to fifteen minutes in 24 per cent., in from sixteen to thirty minutes in 54 per cent., and in from thirty-one to fifty-nine minutes in 21 per cent. The average time was from fifteen to thirty minutes. There was no difference in syphilitic and nonsyphilitic persons. No dye was demonstrable in the urine after from twelve to fourteen hours, and the maximum output occurred after from two to five hours. A comparison of the time of the appearance of the dye in the urine after intravenous and intralumbar injection shows that in the majority of the cases the dye appears after from one and one-half to five minutes when introduced intravenously, demonstrating that it appears in the urine very much earlier when given in this way than when introduced by the lumbar region. Quantitatively, most of the dye introduced intravenously is excreted during the first hour, the curve falling off after this. Experiments were repeated on the same patients in order to determine whether the same percentages would be excreted under the same conditions, and it was found that no variation occurred.

In summarizing, the authors state that foreign bodies introduced into the blood stream pass over into the spinal fluid only in exceptional instances, and are then quickly excreted again. Such substances are esculin, uranin, hexamethylenamin and, exceptionally, arsphenamin. They also conclude that substances introduced in the lumbar region of the spinal canal are resorbed quickly in these regions, and are quickly eliminated.

ALPERS, Philadelphia.

MICROSCOPIC OBSERVATION ON THE CIRCULATION OF THE BLOOD IN THE CEREBRAL CORTEX. HOWARD FLOREY, Brain **48**:43, 1925.

Using cats, rabbits and one monkey in his series of experiments, the author after the usual method of anesthetization made a trephine opening over the cerebral cortex and turned back the dura. For observing the vascular circulation, a 100 candle power Pointolite lamp was used, placed so the beam could be focused obliquely on the opening of the skull. The microscope employed was a spencer dissecting giving stereoscopic vision.

The veins were noted to be much more numerous and formed greater anastomosing circles than the arteries and were more flat in appearance. The large arteries were always superficial to the large veins, and this relationship persisted to the small subdivisions. Vessels of capillary size could be seen both going from the arteries and more numerously entering the veins. The flow of blood could be observed easily in the venous capillaries and smaller and moderate sized veins but not in the larger vessels. In the smallest venous radicles the appearance was that of a succession of "beads" of massed corpuscles, the intervals between which were filled with clear plasma. In some preparations the arteries expanded and the veins lessened in diameter, and this occurred synchronously with the heart beat. A gradual swelling and subsidence in the larger veins synchronous with expiration and inspiration, respectively, was noted.

On experimentation it was found that all the arterial branches from the largest to the smallest reacted to a moderate or vigorous stimulus by a powerful contraction localized only to the point stimulated. All types of veins showed no reaction to mechanical stimulus. Only occasionally was a mild stimulus successful in producing dilatation of the arteries. After the base of the brain

was exposed the basilar artery reacted in the same manner as those of the cortex after mechanical stimulation. The foregoing experiments were repeated using electrical stimuli, and the results were exactly the same. The duration of contraction varied from two minutes to several hours. With thermal stimuli of 41 C., arterial constriction resulted; temperature of 40 C. caused arterial dilatation. With cold, contraction was the usual result.

Epinephrin was applied locally to the cerebral vessels and likewise injected intravenously, and at no time was contraction of a vessel observed. Control experiments on mesenteric vessels resulted in extreme constriction. Pituitary extract behaved exactly as did epinephrin. The author as well as others found that amyl nitrite produced marked dilatation of the arteries. Dilatation of the arteries resulted with all strychnin salts. When the trachea was ligated to produce asphyxia, no contraction or dilatation of the arteries resulted; the veins, however, swelled for a short time. The author calls attention to the fact that while nerves have been described histologically, occurring along the cerebral vessels, no satisfactory evidence has been forthcoming as to their function. When the stellate ganglion was stimulated, neither contraction nor dilatation was noted. The same negative results were obtained when the cervical sympathetic cord was stimulated in a monkey, although the pupil dilated actively to interrupted stimuli, showing that adequate stimuli were being applied to the nerve trunk.

The entire floor of the fourth ventricle was stimulated after a small portion of the cerebellum was removed, but no place was found in which stimulation affected the cerebral vessels. Indirect evidence for the absence of a vasomotor control was given by the fact that production of asphyxia failed to show any active alteration in the caliber of the vessels, though it is known that in such a condition the vasomotor center is actively stimulated. The authors, therefore, conclude that no evidence is forthcoming as to the presence of any nervous control over the caliber of cerebral vessels.

Inflammatory lesions produced experimentally were always localized to the locus of action of the harmful agent.

While admitting that under pathologic conditions, e. g., arteriosclerosis, a spasm of some arteries may occur, the author states that the mechanism by which such could occur is obscure, but that some metabolic product which in a normal condition of the arteries is without effect, in the damaged state may produce contractions.

STACK, Milwaukee.

TWO PRIMARY TUMORS OF THE GASSERIAN GANGLION. ETHEL RUSSELL, J. A. M. A. **84**:413 (Feb. 7) 1925.

The author adds two verified cases of tumor confined to the gasserian ganglion to the few reported in the literature. The condition is rare, the tumors found usually being of an endotheliomatous nature. Of the fifteen cases on record in the literature, one was a bilateral lymphoma (Henneberg), ten were inoperable, and one (Sheldon) was confined to the ganglion alone. The symptom of this tumor is pain confined at first to one division of the trigeminus and later disturbances in other divisions. The pain is unlike that of trifacial neuralgia in its constancy and its association with sensory changes and motor disturbances in the fifth nerve distribution. Dissociation of sensation occurs at times accompanied by anesthesia dolorosa. There may be an associated sixth nerve palsy due to involvement of this structure by the tumor. Sinus disease may be ruled out by the sensory and motor changes

and by careful roentgen-ray and nasal examinations. The author points out that early diagnosis and operative removal must be made in order to extend to the patient the most favorable prognosis, as these tumors are prone to recur and rapidly become inoperable. When involvement of other structures in the middle or posterior fossa occur, surgery offers only palliative relief.

The first case was that of a woman aged 73, who complained of constant pain in the second division of the left fifth nerve, and who developed shortly afterward a left external rectus palsy. Serologic tests were negative. The patient showed no other neurologic involvement than impairment for pain and temperature sense in the second division. There was no motor fifth involvement and no loss of tactile sensation. Operation by Dr. Frazier disclosed an endothelioma, 2 by 2 by 1.5 cm., apparently springing from the second division and following back from the ganglion to the root. The tumor was completely removed, and recovery was uneventful. The sixth nerve paralysis remained, however, and there was total anesthesia to pain, temperature and tactile sensation throughout the distribution of the left nerve following operation.

The second case gave a history of remission similar to true trigeminal neuralgia. The attacks of pain were aggravated by talking and eating, and were confined to the teeth, jaw and tongue on the left side. Alcoholic injections temporarily relieved the pain for a period of seven months, but on its return, an operation was performed by Dr. Frazier. A granulomatous, unencapsulated tumor was found, which took its origin from some structure to the inner side of the ganglion overlying the sensory root. The tumor proved to be endothelial. The patient's recovery was uneventful. The corneal reflex remained active, but there was a loss of tactile, temperature and pain sensation in the area of the third division, some impairment in the second and less impairment in the first.

Of the cases reported in the literature, 25 per cent. proved to be endothelioma, 60 per cent. were left-sided, and it was found that recurrence is the rule rather than the exception in the tumors of this area. The author concludes that primary tumors or sharply localized tumors of the gasserian ganglion are rare, and that surgical treatment is always indicated if for palliative reasons only. The eventual prognosis is grave, since recurrence is frequent.

TEMPLE FAY, Philadelphia.

A STUDY OF THE LIPOIDS IN NEURONIC DEGENERATION AND IN AMAUROTIC FAMILY IDIOCY. E. WESTON HURST, Brain **48**:1, 1925.

The author studied the lipoids in situ microscopically by the use of the various staining reagents, both before and after the tissues were treated with numerous fat solvents, and likewise their staining reactions after mordanting for different periods. The aims of his work were (1) to determine the nature, mode of production and time relation of the various products of nervous disintegration, and (2) to compare the results obtained by the various staining methods in a series of cases and so to ascertain the value of these methods. Normal myelin was found to contain cholesterin, phosphatids and cerebrosids.

A study was made of three cases of tract degeneration caused by hemiplegia and cord compression. In Case 1, a case of hemiplegia lasting six weeks, the products of degeneration were chiefly extracellular, consisting of globules of myelin breaking up into cholesterin, cerebrosids and phosphatids. In Case 2, one of gradual cord compression, of from three to five months' duration, granular

corpuscles had made their appearance, and a good proportion of the fat was intracellular. The bulk of the lipoid consisted of neutral fat and cholesterin with some fatty acid; phosphatids and cerebrosids were found in much smaller amounts. In Case 3, a case of sudden hemiplegia of six months' duration, the lipoids consisted almost entirely of neutral fat and some cholesterin crystals. The fat seen in the granular corpuscles as they approached the Virchow-Robin spaces consisted entirely of neutral fat and fatty acids, the latter being finally converted into neutral fat. The conclusion reached by the author is that neutral fat is the ultimate product of myelin degeneration.

In a case of disseminated sclerosis in which the local toxic onslaught was on the myelin, in studying the periphery of a patch the author found that neutral fat and cholesterin represented the greater part of the lipoid present.

Lipochrome pigment was found in the nerve cells in all cases; this stained readily with all lipoid staining reagents and was extremely resistant to their solvents.

Three cases of neuronic degeneration, two of amaurotic family idiocy and one of cerebral macular degeneration were then studied, and the nature of their products of degeneration investigated. In all three the lipoids were found to consist chiefly of cerebrosids and phosphatids, but those in the latter case differed in that the lipoids stained deeper with sharlach, and were practically insoluble in all fat solvents. After various reasoning, and recalling the similarity in the two diseases from a clinical and pathologic standpoint, the author concludes that each of these degenerations is essentially the same, and that the differences that exist are due solely to the acuteness or chronicity of the process. In amaurotic family idiocy cerebrosids and phosphatids are liberated in a readily soluble form and possess staining properties more or less typical of the groups. In cerebromacular degeneration and in senile nerve cells studied, they are so altered as to become insoluble in the fat solvents and to stain deeper with sharlach. Attention is called to the similarity of the lipoids in the latter two cases in which the degeneration is of a slower production.

As to the origin of the lipoids studied, the author ascertained that in normal myelin the lipoids exist as such and are not in the form of an emulsion or in union with protein. The lipoids of cerebrosids and phosphatids found in the cell protoplasm in the foregoing forms of neuronic degeneration the author concludes have been liberated from chemical combination with some other cellular substance, and as it is known that they unite readily with protein, it may be assumed that they exist in the form of lipoproteins.

STACK, Milwaukee.

A CASE OF OLIVO-PONTILE CEREBELLAR ATROPHY AND OUR CONCEPTIONS OF NEOCEREBELLUM AND PALEOCEREBELLUM. C. WINKLER, Schweiz. Arch. f. Neurol. u. Psychiat. Festschr. f. Constantin v. Manokow **13**:685-702, 1923.

The pioneer work of Bolk and Elliot Smith disproved the existence of any fundamental difference between vermis and cerebellar hemispheres. This resulted in a new nomenclature; however, it failed to smooth out all discordance; facts of comparative anatomy, gathered by Edinger and his school, tended to show that the vermis together with the flocculus represented a phylogenetically older part, the paleocerebellum, whereas the hemispheres, having a more recent phylogenetic history, were looked on as the neocerebellum; cases of neocerebellar atrophy furnished a pathologic basis for this contention; the studies by Obersteiner and von Valkenburg on myelinization brought a corresponding results from the embryologist.

The concept of neocerebellum and paleocerebellum represented real progress. The question arose, however, as to whether the neocerebellum was an organ placed altogether in opposition or whether, as Jelgersma and others supposed, this structure might also have grown into the paleocerebellum by intussusception.

Winkler's case was that of a man, aged 59, who suffered from cerebellar ataxia and disorders of speech. A brother was similarly afflicted. Necropsy disclosed some rather interesting findings. The inferior olivary nuclei and the arcuate nuclei appeared externally to be well preserved, however, almost no nerve cells were found there microscopically. The external arcuate fibers were totally absent; there were no fibers in the hilus olivae, none crossing the medial lemniscus, none passing through the spinal tract of the fifth nerve and the pedunculi corporis restiformis, and none in the raphé running from the arcuate nuclei to form the striae medullares of the fourth ventricle. Sections through the restiform body resembled those of a 42 cm. fetus, in which only the dorsal spinocerebellar tract is myelinated. There was a marked loss of cells and a complete absence of transverse fibers in the ventral part of the pons and in the middle cerebellar peduncle. In the cerebellar cortex, there was a loss of the intragranular fibers, whereas the tangential pericellular fibers were relatively well preserved.

A lesion of the neocerebellum, which he assumed this to be, apparently destroys all neocerebellar paths with their arborizations, which, according to these observations, are the intragranular or moss fibers. A certain number of synapse cells, in this case dwarf cells in the molecular layer, and a few Purkinje cells, were involved, but most of these escaped degeneration. According to Essick, in a 23 mm. fetus there may be seen an enormous proliferation of cells in the region of the dorsal nucleus of the eighth nerve; these leave their place of origin and migrate in part to the olivo-arcuate position, forming the corresponding nuclei, and in part to the pons to form the ventral pontile nuclei. It is supposed that in certain cases these younger cells are less resistant than the older structures, and therefore they die relatively early.

In its outward appearance, this conception does not agree with the popular scheme of neocerebellum and paleocerebellum. The paleocerebellum may prevail in the midline, but a large part of the neocerebellum is represented here also and must be interpolated between older structures: in the same way paleocerebellar elements must be intermingled with the neocerebellar structures of the lateral hemispheres; even in the flocculus, a small amount of neocerebellar structures may be found.

WOLTMAN, Rochester Minn.

ACUTE TOXIC MENINGO-ENCEPHALITIS OF OTORHINOGENIC ORIGIN. C. F. YERGER, Arch. Otolaryngol. **1**:198 (Feb.) 1925.

This is a well written and concise article calling attention to the fact that in toxemic conditions we may find that the central nervous system is involved, as evidenced by the rigidity of the neck, Kernig's sign and other signs of meningitis, with slight changes in the spinal fluid. These cases the author believes are something more than a serous meningitis. The brain substance is affected by the toxemia, and we should therefore consider them as cases of toxic meningo-encephalitis. The importance of this point of view is that cure of the source of toxemia relieves the condition, whether it is caused by a respiratory infection or by a focus in the ear or nose. With a clear understanding of the spinal fluid findings in these cases, in some cases diagnosed as otitic brain abscess there will be no unnecessary exploration, and in other

cases in which the surgeon thinks that operation is useless because a suppurative process has begun, the patient will be saved by timely operation.

The main point in the differentiation of these cases from other conditions giving meningeal symptoms is the study of the spinal fluid. In meningismus the spinal fluid is normal, according to the author; in serous meningitis the fluid is either normal but under increased pressure or abnormal with increased cell count, consisting of lymphocytes, globulin is present, but no bacteria; in toxic meningo-encephalitis the fluid is under increased tension, positive globulin, an increased cell count, mostly lymphocytes, approximately 10 to 100 cells, bacteria absent; in sympathetic meningitis (Plaut and Schottmüller) there is increased pressure with an increased cell count, variable in amount, usually ranging from 250 to 3,000 cells and mostly of the polymorphonuclear type, globulin is more marked, bacteria are absent; in acute diffuse suppurative leptomeningitis, globulin is marked, there are many cells of polymorphonuclear type usually in excess of 3,000 and often bacteria.

The onset may be sudden or gradual. There may be convulsions, headache, vomiting, vertigo, photophobia and delirium acute and stormy, replaced later by stupor or coma. The deep reflexes become abolished. After the focus is cleared up, all these symptoms disappear either suddenly or in the course of a week. If the focus is not cleared up, the patient dies, either from toxic meningitis, septic meningitis, sinus thrombosis or brain abscess.

The author calls attention to those cases in which there are no signs of meningitis, but in which the spinal fluid shows an increased cell count (20 to 250 cells) globulin, slight pressure, but no bacteria. He has found this in extradural abscess, brain abscess, cerebrospinal syphilis, epidemic encephalitis, poliomyelitis and poliomyelitis superior and acute toxic meningo-encephalitis.

PHYSIOLOGY OF THE LABYRINTH. J. GORDON WILSON, Arch. Otolaryngol. **1**:231 (Feb.) 1925.

This is an abstract of the summary of the work of Magnus and de Kleijn on the Function of the Semicircular Canals and the Otolith Organs, a paper by Maxwell on habituation to rotation and a paper by Dodge on the threshold of rotation.

HUNTER, Philadelphia.

THE INFLUENCE OF EMOTIONAL STATES ON THE BASAL METABOLISM. LLOYD H. ZIEGLER and B. S. LEVINE, Am. J. M. Sc. **169**:68 (Jan.) 1925.

The observation that the basal metabolic rate is often elevated in psychoneurotic persons without goiter prompted the authors to study a series of psychoneurotic patients while under slight emotional strain. Three readings were taken, all identical except that during the second test the patient was requested to think of some fact taken from the history which would seem to produce an emotional response. Careful notes were taken during the second period regarding the external signs of the patient's subjective feelings. Fourteen cases were so studied. The first patient was 34 years old and had a condition diagnosed anxiety hysteria. He had had many unpleasant army experiences, so he was asked to think over these during the second test. During the reading his face became flushed, breathing irregular, and he had fine tremors over the upper half of the body. There were a few facial grimaces. Subjectively, he admitted that he was disturbed emotionally. He could feel his heart beating faster and had a dull sensation in the heart region. The basal metabolic reading on the first control was +9.62, the second test showed

a reading of +28.9, while the third reading or second control was +13.9.

The second patient whose case was diagnosed as anxiety neurosis was told to think of his unpleasant army experiences. He had flushing of the face, heavy breathing, tremor of the upper extremities and finally came to tears. His breathing then became irregular. Subjectively, he admitted that he felt depressed and that his emotions became intense. His reading in the first control was —2.8; during the emotional strain it was +40, while the second control showed a +8.

Twelve other cases were similarly studied, in four of which the condition was diagnosed as anxiety hysteria, in three as hysteria, in two as neurasthenia and in two as constitutional psychosis, one with depressive and anxiety features and one with schizophrenic features. All patients showed some slight external evidence of increased emotility during the second observation, but only two were definitely restless. The second basal reading was elevated above that of the controls in all but two cases, in which there was a decided drop. In one of these cases there was an anxiety hysteria and in the other constitutional psycopathy with schizophrenic features.

The experiments clearly show that a neurasthenic person may dissipate energy without realizing it. By comparative study it was shown that emotional reactions in the patients in terms of expended energy were equivalent to one-half that necessary for the same patient to do the work of a merchant tailor. The necessity for watching the patient's emotion during the metabolic readings is emphasized. Unless something is known about the life problems of the patient and their effects on him, mistakes of diagnosis may easily follow the basal metabolic determination. It is pointed out also that there should be further study of exophthalmic goiter to determine which components are due to secretion of the thyroid and which may be due to lowered threshold of emotional reactivity.

WILSON, Clifton Springs, N. Y.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

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WILLIAM HEALY, M.D., *President, in the Chair*

SPINAL FLUID PRESSURE READINGS IN EPILEPSY. DR. WILLIAM G. LENNOX.

It has long been known that marked increase in intracranial pressure causes convulsions. Recently one writer (Leriche) stated that hypotension also may be a factor in the production of convulsions. Weed and others suggested alteration of intracranial pressure (by use of hypertonic or hypotonic solutions) as a method of treatment of epilepsy. For these reasons it is important to determine whether there is abnormality in the pressure of the spinal fluid of persons subject to recurring convulsions.

Of the thirty-three patients we have examined to date, almost all have had normal spinal fluid pressures. In six instances, the initial pressure was 200 mm. of spinal fluid or more. Spinal drainage was performed on a number of these patients without a resulting change in the number of convulsions. In one case of status, however, there was complete cessation of seizures for a period of eight hours following the drainage. During the preceding eight hours there had been nineteen seizures. In this patient pressure of the spinal fluid was observed during seven convulsions. During the tonic stage of the more severe of the convulsions the spinal fluid pressure increased nearly 600 mm., to a height of more than 700 mm. There was not an initial fall of pressure, but observations made twenty-four hours later (when the initial pressure was low) showed a fall at the beginning of the convulsions to a negative pressure of 50 mm. It is suggested that the marked fluctuations observed were the results of changes of intrathoracic pressure. These observations are to be extended to a large series of cases.

DISCUSSION

DR. H. C. SOLOMON: Does Dr. Lennox or Dr. Mella feel that there is any relation between glioma and epilepsy? Regarding the question of pressure findings: In these attacks of a convulsive nature, the pressure rises as high as 700 mm. in a partial open system. What effect does that have on the brain ventricles? Does this lead to hydrocephalus?

How high does the pressure rise in an ordinary sneeze? Sometimes it will rise to more than 500 mm., which gives us some idea of the amount of trauma the brain endures in daily affairs. In these high pressures what happens to the mechanism of the brain? There is some sort of equilibrating mechanism whereby cerebrospinal fluid tends to keep a definite base level, and that level varies markedly with some patients. Some have a base level of over 100 and some of 200, but they tend to reestablish themselves by some mechanism of which we have no record. In this particular case of epilepsy, what happens to this mechanism whereby equilibration is brought into play? We know nothing of the equilibrating mechanism of the cerebrospinal fluid pressure whereby it tends to stay more or less at a constant level and does not vary much except for momentary oscillations.

DR. LENNOX: Necropsy of a patient from whom the observations of spinal fluid pressure during convulsions were obtained showed a glioma of the temporal lobe with extension into the pia covering the brain. The tumor offered no explanation either for the convulsions, which had begun about eight or ten years before, or of the cause of death. It is doubtful whether dilated ventricles are the result of the increased cerebrospinal fluid pressure during convulsions. At least, Cobb's rabbits, which had been subjected to convulsions over a considerable period of time, showed no such dilatation.

THE THERAPEUTIC USE OF DEHYDRATION IN HYPOMANIA. DR. DONALD GREGG.

From the pathological laboratory are reported two observations which have been accepted without question: 1. Many cases of alcoholic delirium coming to necropsy show wet brains. 2. Experimentally, brain bulk can be reduced by the administration of hypertonic salt solution. The latter observation has been utilized in brain surgery. Whether there is any correlation between increased brain bulk and excessive mental activity, such as is commonly seen in hypomania, is an interesting speculation. Clinically, many procedures which presumably lessen cerebral congestion and brain bulk have been used with successful, although often temporary, results. Dr. Donald Munro reported last month on the beneficial results of lumbar tapping in cases of injury of the head. Cases of alcoholic delirium are often temporarily helped by lumbar puncture. The old "relief station cocktail" containing a strong dose of Epsom salts has benefited many an alcoholic patient, if not promptly lost. The hot pack and the prolonged warm bath have an undoubted sedative effect, and presumably draw fluid from the cerebral region to the body and limbs. The mustard foot bath and the warm bath at bed time are time honored remedies. Cerebral congestion can probably be somewhat reduced by skilful massage. Whether the beneficial results of an effective dose of castor oil sometimes seen are due to relief from so-called auto-intoxication or to dehydration has not yet been determined. Having in mind these laboratory and clinical observations, the following case is interesting.

Mr. X., aged 23, of excellent Anglo-Saxon stock, was recently brought to me for treatment in a typically hypomanic condition. His family history disclosed no reason for his condition because of inheritance. His past history showed that he had had no previous attacks of excitement or depression. Ordinarily, he was quiet and shy, interested in artistic and intellectual activities, but without evident productive ability in artistic, musical or literary lines. He had previously had no stirring sex activities and no handicapping physical infections. His life during his college years and his relations with his family had not aroused criticism or comment. He was considered a normal young man. About a week before coming under hospital care, he had become excited, talkative and restless. He conversed for eighteen hours at a stretch with a college classmate. He wrote out in detail his sensations and activities during twenty-four hours, and thought that his experience should be expanded into book form and printed, and that it would have a tremendously important influence in redeeming the world from its present difficulties. He had developed his physique marvellously in a week. He had discovered in himself an unsuspected ability to compose music and to sing. He possessed perfect pitch. Running through his excitement was a strong sex activity. With some difficulty he was persuaded to get to bed and was urged to try the effect of the horizontal position on his mental activities. Physical examination showed a

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Monthly Meeting, March 19, 1925

WILLIAM HEALY, M.D., *President, in the Chair*

SPINAL FLUID PRESSURE READINGS IN EPILEPSY. DR. WILLIAM G. LENNOX.

It has long been known that marked increase in intracranial pressure causes convulsions. Recently one writer (Leriche) stated that hypotension also may be a factor in the production of convulsions. Weed and others suggested alteration of intracranial pressure (by use of hypertonic or hypotonic solutions) as a method of treatment of epilepsy. For these reasons it is important to determine whether there is abnormality in the pressure of the spinal fluid of persons subject to recurring convulsions.

Of the thirty-three patients we have examined to date, almost all have had normal spinal fluid pressures. In six instances, the initial pressure was 200 mm. of spinal fluid or more. Spinal drainage was performed on a number of these patients without a resulting change in the number of convulsions. In one case of status, however, there was complete cessation of seizures for a period of eight hours following the drainage. During the preceding eight hours there had been nineteen seizures. In this patient pressure of the spinal fluid was observed during seven convulsions. During the tonic stage of the more severe of the convulsions the spinal fluid pressure increased nearly 600 mm., to a height of more than 700 mm. There was not an initial fall of pressure, but observations made twenty-four hours later (when the initial pressure was low) showed a fall at the beginning of the convulsions to a negative pressure of 50 mm. It is suggested that the marked fluctuations observed were the results of changes of intrathoracic pressure. These observations are to be extended to a large series of cases.

DISCUSSION

DR. H. C. SOLOMON: Does Dr. Lennox or Dr. Mella feel that there is any relation between glioma and epilepsy? Regarding the question of pressure findings: In these attacks of a convulsive nature, the pressure rises as high as 700 mm. in a partial open system. What effect does that have on the brain ventricles? Does this lead to hydrocephalus?

How high does the pressure rise in an ordinary sneeze? Sometimes it will rise to more than 500 mm., which gives us some idea of the amount of trauma the brain endures in daily affairs. In these high pressures what happens to the mechanism of the brain? There is some sort of equilibrating mechanism whereby cerebrospinal fluid tends to keep a definite base level, and that level varies markedly with some patients. Some have a base level of over 100 and some of 200, but they tend to reestablish themselves by some mechanism of which we have no record. In this particular case of epilepsy, what happens to this mechanism whereby equilibration is brought into play? We know nothing of the equilibrating mechanism of the cerebrospinal fluid pressure whereby it tends to stay more or less at a constant level and does not vary much except for momentary oscillations.

DR. LENNOX: Necropsy of a patient from whom the observations of spinal fluid pressure during convulsions were obtained showed a glioma of the temporal lobe with extension into the pia covering the brain. The tumor offered no explanation either for the convulsions, which had begun about eight or ten years before, or of the cause of death. It is doubtful whether dilated ventricles are the result of the increased cerebrospinal fluid pressure during convulsions. At least, Cobb's rabbits, which had been subjected to convulsions over a considerable period of time, showed no such dilatation.

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well developed young man without evidence of physical infection or deformity. His tendon reflexes were generally increased. He was 15 or 20 pounds (6.8 or 9 kg.) under his normal weight. His pulse rate was markedly variable. His systolic blood pressure was 155. He was given an ounce of magnesium sulphate in warm saturated solution by rectum. The result of this injection was a copious watery movement twenty minutes later, followed by another dejection after three hours. He slept six and a half hours that night without other medication. The next morning he was much quieter and somewhat clearer. He was willing to remain in his room quietly, spending most of his time in bed. The injection of magnesium sulphate was repeated that evening with a double dejection resulting. The next afternoon he was sent for a walk in the woods with a nurse, after a calm forenoon. In the evening he was given a third injection of magnesium sulphate. He slept eight and a half hours that night. The next morning he showed considerable insight. He said that his feet were on rock bottom again. Since then convalescence has continued uneventfully. At the end of a week his father thought him as normal as before his illness. In four days he gained 8 pounds (3.6 kg.). His blood pressure dropped to 135 systolic.

This case is reported as one showing typical symptoms of hypomania, but of unusual brevity. Improvement followed immediately after moderate dehydration with magnesium sulphate. Whether this dehydration bore any relation to the unusually rapid improvement is problematical. Dehydration with magnesium sulphate by rectum is, however, so simple in application and seemingly so innocuous that it deserves further trial.

DR. E. W. TAYLOR: Dr. Solomon has just stated to me that he had a patient at an institution who came out of a hypomanic state in forty-eight hours without any medication. I should suppose that theoretically this method might be indicated but that one should have a very large number of cases before drawing any deductions. Improvement was most striking in this instance.

DR. E. S. ABBOT: How much intake of water was there along with the expulsion of water. If the man gained 8 pounds in four or five days, a considerable portion of that must have been fluid. The question is: How much actual dehydration of the body was there, and how long did it last?

DR. F. H. PACKARD: I occasionally see patients brought to the hospital in an excited state, whose condition clears up almost over night without any particular treatment, and no evidence of psychosis is longer manifest. When this occurs, as a rule it is in patients with whom the onset has been sudden. They seem to be manic episodes.

DR. GREGG: Answering some of the questions raised in the discussion, it seems to me that as the magnesium sulphate was expelled in twenty minutes with much acompanying fluid, not much, if any, of the drug could have been absorbed to produce a systemic effect. I have not yet had an opportunity to try this treatment in a chronic case. To be sure, not infrequently cases of acute excitement are seen that clear up rapidly. Some patients are given purgatives and some hot packs, which are methods of dehydration more difficult to give than the treatment suggested in this paper. No conclusions are drawn from the experience reported in this single case; I merely suggest that the favorable results produced by eliminative treatment in the deliria may be due primarily to dehydration of the brain.

CAUSES OF FEEBLEMINDEDNESS. DR. ABRAHAM MYERSON.

The literature of psychiatry and syphilis is almost unanimous in the belief that syphilis causes feeblemindedness. That syphilis causes mental disease of the type exemplified by general paresis, and which is in its essentials inflammatory in nature, is, of course, undoubted. That it can cause an amentia, a retarded mental development, has not been proved.

In recent years, a good deal of work has been done on the Wassermann reaction in the schools for the feebleminded. An interesting thing is noted. In the early days of the Wassermann reaction, and when small groups of the feebleminded are taken, the literature seems to show an excessive amount of syphilis in the schools for feebleminded. On the other hand, in the recent literature, and wherever large groups of the feebleminded are studied and compared with large groups of the nonfeebleminded population, there seems to be no essential numerical difference in the amount of syphilis. Thus, of the 3,911 inmates of the hospitals for the feebleminded in Massachusetts, that is, Waverley, Wrentham, and Belchertown, there is a total of 143 with positive Wassermann reactions, which is a percentage of 3.6. A survey of the literature seems to indicate that that is about the percentage of positive Wassermann reactions in the large institutions in which the Wassermann work has been done in a reliable way.

When an effort is made to check this up by a survey of the amount of syphilis among the normal, or nonfeebleminded, population, difficulties are encountered in the selection of cases, which has usually been among the sick, and by the fact that in each stratum of the population the amount of syphilis seems to vary, so that in the higher social and cultural groups there is distinctly less syphilis than there is in the lower social and cultural groups. Most of the feeble-minded in Waverley, Wrentham and Belchertown come from the lower social groups, in many cases from the very lowest, and on the whole, it may safely be said that the number of patients with positive Wassermann reactions in these institutions is not greater than that in the child population as a whole. Thus, from the statistical standpoint alone, the evidence for syphilis as a cause of feeblemindedness is slight.

Another way of attacking the problem is the clinical examination of those in the institutions who have positive Wassermann reactions. This was done in fifty-eight of the sixty-five patients with positive tests at the Waverley School for the Feebleminded. Of the fifty-eight patients, there were twenty-one in whom the hutchinsonian signs were present in greater or lesser degree. I included as hutchinsonian signs only those which definitely belong to this syndrome, since abnormalities of all kinds have often been classed as syphilitic, which are present in nonsyphilitic persons in almost an equal amount. Definite neurologic signs were found in fourteen cases, but these neurologic signs were, in the majority of cases, by no means conclusive evidence that the patient had neurosyphilis, because they are common among the feebleminded, and even among the normal; for example, strabismus occurred four times without paralysis and without other associated neurologic signs, and there were half a dozen cases of slight irregularities in the pupils with negative Wassermann tests of the spinal fluid. Wherever there were definite signs of neurosyphilis, there was paresis or some condition similar to those found in the adult, and in these cases the spinal fluid was positive. In other words, these were not cases of *amentia*, but, so to speak, of *dementia*. Of the fourteen lumbar punctures that were made, all were negative with the exception of three, and in

two of these the Wassermann test was positive, in one it was doubtful. There was some change in the albumin and globulin tests. In other words, the examination of these patients, in the vast majority of cases, showed no definitely well recognized signs of syphilis of the nervous system.

The incidence of definitely known feeblemindedness in the ancestors was twelve. By ancestors is meant here father or mother or both. The number of cases in which the family history was unknown, owing to the fact that the children had been abandoned, and in which the circumstances were strongly suggestive of very low moral, and probably mental, status in the parents, was twelve. Cases of extremely low social and moral standing, aside from the cases already cited in which the mental status of the parents could not be determined, but in which there was good reason to believe it was low, were eight. Cases in which one or more siblings were feebleminded and in hospitals for the feebleminded totaled ten. All of these facts put together make it seem more likely that in these cases, at least, the cause lay in familial situations rather than in syphilis; in other words, syphilis was coincidental, rather than causative. In at least six of the sixty-five cases there was every reason to believe that the syphilis was acquired, since these were young women whose sex career before they came to the hospital was distinctly promiscuous.

In the cases in which there was no family history to indicate a cause, and in which there was no evidence of neurosyphilis of any kind, there was, on the whole, nothing to distinguish the feebleminded person from the mass of the feebleminded of the institution. There was one Mongolian; there were two dwarfs, strongly suggesting endocrinologic disturbances of some kind. Several of these persons with positive Wassermann reactions were typical low-grade idiots, with the coarse features, brush-like hair, cyanosed hands and automatic movements resembling what Dr. Fernald often called the "blue-sky idiot," i. e., coming from normal families. In other words, these cases indicated the same kind of problems that unknown feeblemindedness does, and so far as our present experience goes, they were not present in greater or lesser number than in the mass of the population at Waverley.

As a sort of check on these cases, some records of Dr. H. C. Solomon's clinic were studied. Of the forty-seven patients with congenital syphilis under treatment at his clinic, there were eight juveniles with paresis, one patient with neurosyphilis, three with doubtful mentality, twenty-eight normal persons, one with unknown mentality, and six mentally defective. Of the mentally defective in the Solomon cases, one had a father who was in prison for manslaughter, three had mothers who were definitely mentally defective, and one had a mother and father of low grade; in other words, in these six cases, there were at least four in whom the ancestors alone would have been regarded as cause enough for the feeblemindedness in the descendants.

In the neuropathology of "syphilitic feeblemindedness" one is impressed with the paucity of material studied. It may be stated that no real study of any importance has been made. Most of the studies have been made on the fetus or on the extremely young infant. In such cases there is an active neurosyphilis and active general syphilis. Wohlwill's study seems to me to indicate that in the older children there is no definite evidence that any retardation or developmental anomaly of the brain has been caused by syphilis. In other words, pathology does not help us, as yet, in determining whether or not syphilis can retard mental development, since the only material studied has been that of infants overwhelmed by syphilis either prenatally or shortly after birth.

Conclusion: That syphilis causes mental defectiveness, aside from the rare cases of juvenile paresis, has not been proved. On the whole, the evidence is rather against this point of view than for it.

(NOTE.—This is the first of the papers representing the research of the Commonwealth of Massachusetts on the causes of feeblemindedness.)

DISCUSSION

DR. G. L. WALLACE: A considerable number of our patients with syphilis have acquired the disease. This is especially true of the girls. I am not prepared to say exactly how many. In connection with Dr. Myerson's survey, which reduces to a minimum syphilis as a causative factor for feeblemindedness, I question a little whether, in the debilitating effect syphilis may have on the progenitors, is may not be responsible indirectly, to a degree, for mental defect when no positive reaction is obtained. But his findings agree with our observations, that the majority, excluding the comparatively few pathologic cases of mental deficiency, are simply as Dr. Fernald used to express it, a question of a lesser degree of intelligence. Dr. Myerson's findings in this particular, in not making syphilis responsible for as large a number as we used to think before the Wassermann tests were taken on our patients, is rather in line with the observations of Dr. Fernald and a good many others.

DR. WILLIAM HEALY: A few years ago at the University of Chicago a prolonged bit of research was done by Dr. Stevens along these lines. He did his work curiously it seemed to me. He held syphilis responsible for a great deal of feeblemindedness, between 30 and 40 per. cent. I was very much amused because just about the time he came out in favor of this high percentage, there appeared the report of work from Denmark which falls in closely with what Dr. Myerson says, and the percentage of possible responsibility of syphilis for feeblemindedness was, if I remember it correctly, less than 5 per cent. I know it was extremely low. We are up against the fact, as Dr. Myerson says, that the Wassermann test does not always show a positive reaction, and we have to fall back on the so-called stigmas, particularly on hutchinsonian teeth, and there we come to a peculiar difficulty because nobody has ever yet accurately determined what syphilitic teeth really are. I have talked with many on that subject, and, strangely enough, few people in this country seem to be aware of the apparently important work of Cavallaro, which was translated and which appeared in the *Dental Cosmos* of 1913, with copious illustrations. He maintained that he had been able to discover in congenital syphilitic fetuses much evidence of infection of the dental alveoli, and that this was present at its maximum at the third month of intra-uterine life, when the anlage of the second incisors and cuspids was forming. This is an interesting study. The upshot of his paper is what we call hutchinsonian teeth; the peg-shaped incisors with crescentic erosions are by no means the only kind of teeth indicative of syphilis. What kind of teeth are indicative of congenital syphilis remains a matter of some doubt.

DR. MYERSON: One is rather surprised that there is no greater percentage of positive Wassermann reactions among these children. The families from which they come, in very large numbers, live in the most deplorable social and cultural conditions, and in very many cases sex life begins early. The sex life of the mother and father both are promiscuous, so that the number of positive Wassermann tests might easily relate to the types of life the parents led. About hutchinsonian teeth, those I accepted as hutchinsonian were the definite and well-known types with concave margin of incisors and peg-shaped bicuspids.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 27, 1925

SHERMAN F. GILPIN, M.D., *President, in the Chair*

STUDIES ON THE CEREBRAL VASCULATURE BY MEANS OF THE ROENTGEN RAY: A PRELIMINARY REPORT. DR. TEMPLE FAY.

The study consisted of a series of fifteen brains into which opaque material had been injected with special reference to: (1) the degree of anastomosis existing between the larger groups of vessels, (2) the determination of the degree and extent of end arteries in the brain, (3) the estimation of relative vascularity in various portions of the brain, (4) studies of the distribution of the anterior cerebral arteries.

The technic employed on the first five brains consisted of injections of metallic mercury introduced into a single artery, such as the middle cerebral artery of one side, after careful ligation of all communicating branches about the base including the circle of Willis had been accomplished. A pressure of 200 mm. of mercury was used, this figure being chosen as the "top normal" point at which arterial tension might exist in the individual. Into the second series, consisting of ten brains, were injected barium sulphate introduced into the femoral artery, so that the entire arterial circulation was made opaque to the roentgen ray. The brains of these specimens were removed after two weeks of hardening, and stereoscopic roentgen-ray studies were made, both lateral and vertical, on all fifteen specimens. Rather marked collateral circulation was found over the cortex between the anterior, the middle and posterior cerebral arteries in fairly definite areas. End arteries were confined chiefly to the subcortical vasculature, especially that of the basal ganglia. It was impossible to inject one of the arteries mentioned above with mercury, without rapid diffusion of the liquid into the adjacent arterial zones. *A relatively avascular area* appears to exist from a point about 2.5 cm. on either side of the midline, and extending from the frontal pole well into the parietal lobe and parallel to the midline, a finding which may have significance in cases in which transcortical approach for tumor is to be made to the deeper structures. The peculiar arterial distribution to the frontal lobes by means of the anterior cerebral arteries seems to indicate that these structures were laid down in the phylogenetic plan of development before the subsequent development and enlargement of the frontal lobes in man. The arterial branches of the middle and posterior cerebral arteries course more directly to their determination than do those of the anterior cerebral. The latter pass out over the frontal lobe and throw down arterial loops as though compensating for a more recent development of this portion of the brain, which has demanded increasing vascular supply. The foregoing studies are preliminary to a more extensive scrutiny of the individual areas of the brain. A further report of the subcortical distribution will be made at some future date.

DISCUSSION

DR. WILLIAM G. SPILLER: The method which Dr. Fay has followed for the study of the vessels of the brain is entirely original with him, and is very ingenious. He has shown clearly the extensive anastomosis which occurs in the vessels of the cortex of the cerebrum, but he believes that the arteries entering the interior of the cerebrum are terminal vessels.

Dr. Beevor presented his injected specimens of the brain before the American Neurological Association, and I well recall those splendid preparations. He also showed that when injection is made into a cortical artery the supply as indicated by the injection is extensive. He used fluid gelatin of different colors and made injections into the vessels simultaneously and under equal pressure.

Dr. Fay has carried on his work without counter pressure in the surrounding vascular supply. There seems to be considerable opportunity for investigation in the method he has originated, but neither he nor Dr. Beevor made injections into the basal parts of the brain, only into the cerebrum. It is desirable to have a definite description of the vascular supply of the brain stem. I have made some investigation of the syndromes produced by occlusion of different vessels of the brain and spinal cord, such as occlusion of the vessels supplying the lenticular nucleus, of the vessels supplying the oculomotor nuclei, of the vessel supplying the lateral part of the medulla oblongata, of the vessels supplying the median portion of the medulla oblongata and of the vessels supplying the anterior portion of the cervical spinal cord. It is to be hoped that Dr. Fay will continue his work and give us information of the vascular supply of the basal parts of the brain and cerebellum. His work would be increased in value if he could limit the area into which injections are made, possibly by graduating the degree of pressure during the injection.

The value of careful study of the vascular distribution of a definite part of the brain has been shown recently by Foix, Hillemand and Schalit (*Rev. neurol.*, February, 1925) in their study of the vascular supply of the lateral part of the medulla oblongata and the discovery of the small vessel at the lateral part of the medulla oblongata which they have called the artère de la fossette latérale du bulbe.

A Case of Acute Ascending Paralysis. Dr. F. H. Leavitt.

This case is presented because it showed an acute ascending paralysis which began in the legs and caused death from respiratory paralysis in three days, without alteration of consciousness.

The patient had had kidney disease for a number of years. On March 8, 1924, she fell down a flight of steps on the stage of a theater in Philadelphia, during her employment there as an actress. She was bruised but returned to work in three days, but was unable to dance because of "stiffness" in both legs. On March 21, 1924, she had a febrile illness, characterized by sore throat without exudate, bronchial irritation, general body aching, and fever, all of which completely disappeared in two days. On March 28, 1924, while walking, she suddenly became weak in both legs and was unable to walk again.

When she was seen three hours later, she was unable to stand, although she could move all the muscles of the lower extremities. Both knee and achilles reflexes were hyperactive and equal without spasticity, ankle clonus, or Babinski's sign. Touch, pain, heat and cold and joint sense were normal throughout. The nerve trunks were not tender. The pupils, cranial nerves, speech, vertebrae, sphincteric action and temperature were normal. The heart action was irregular, and the first sound lacked muscular tone; the blood pressure was: systolic, 158, diastolic, 80. At this time there was no difficulty in the use of the muscles of any other part of the body.

By noon of the next day, both legs were almost totally paralyzed, the weakness being most marked distally, and there was extreme weakness of the muscles of the trunk and of both arms. The tendon reflexes of both legs and of both arms were decreased, respiration had become difficult, and the breathing

was jerky and almost entirely diaphragmatic. Speech was weak, due mainly to dyspnea; dysphagia was present, and movements of the tongue were limited. The patient was alert mentally and kept repeating "I cannot breathe." She presented a picture of total motor paralysis of the arms, legs, and body with perfectly clear consciousness. The blood pressure had risen to systolic 200, diastolic 110, but the heart action was regular and the lungs were normal. The patient died on the third day from respiratory paralysis; her heart continued to beat for some minutes after respiration failed, and consciousness was preserved almost to the last minute.

Laboratory Examinations.—The blood Wassermann test was negative. The findings in the urine were those of chronic parenchymatous nephritis. Blood chemistry revealed: glucose, 142 mg. per 100 c.c.; nonprotein nitrogen, 35 mg. per 100 c.c.; urea, 19 mg. per 100 c.c.

Pathologic Report.—In the kidneys were found the seat of chronic parenchymatous degeneration and chronic interstitial hepatitis and splenitis. No gross pathology was noted in the brain, but the spinal cord appeared to be diffusely swollen and white; there were no signs of hemorrhage or gross damage to the brain or spinal cord.

Dr. W. G. Spiller, who made a miscroscopic examination reported: Sections were examined from the spinal cord, medulla oblongata and pons, and no distinct lesions were found. The Marchi stain showed no degeneration of the nerve fibers. The Nissl stain showed that the cells of the anterior horns were in good condition. They were well pigmented but not abnormally so. The cells of the anterior horns of the cervical region were possibly not as numerous as they should be and presented a shrunken appearance, but it is impossible to believe that such changes could occur within three days. There were no chromatolysis and no nuclear displacement, nothing suggesting axonal degeneration. The Alzheimer-Mann stain showed more medullary sheaths deeply stained in pink than might be considered entirely normal, but a similar condition was found in the cervical region, and it is questionable whether this staining could be considered pathologic. The axis cylinders did not show any tendency toward red coloration. The medulla oblongata presented some nerve cells in process of degeneration, but this may be a finding in any normal medulla oblongata.

The absence of degenerative changes is to be explained by the short duration of the process. The paralysis began gradually on a Friday afternoon, became complete paralysis of the limbs, and death occurred early the following Tuesday morning. The time was too short to permit degenerative changes to become distinct. There were no signs of an inflammatory condition.

LUMBAR PUNCTURE HEADACHE. DR. BERNARD J. ALPERS. This paper will appear in full in a later issue.

A SHORT RÉSUMÉ OF WORK FROM THE NEUROPATHOLOGICAL LABORATORY OF THE LABORATORY OF THE PHILADELPHIA GENERAL HOSPITAL. DR. R. B. RICHARDSON.

Book Reviews

CLINICAL PSYCHOLOGY. By LOUIS E. BISCH, M.D., PH.D. Cloth. Price, $3. Pp. 346. Baltimore: Williams & Wilkins Company, 1925.

The title is something of a misnomer, since the book is devoted largely to a popular presentation, with ample excerpts from the literature, of the problem of feeblemindedness and the use of the Binet-Simon tests of intelligence. Results of these tests seem to play the all-important rôle in the fifty-eight illustrative case studies from the records of Dr. Schlapp's clinic for mental defectives at the New York Postgraduate Medical School. A good bibliography of the principal English works in clinical psychology has been prepared for appendix B by Mrs. Barrows. The body of the book is based on a course of lectures to students at Teachers College of Columbia University.

The writer shows definite appreciation of the complex etiology of abnormal behavior of children, and stresses the importance of medical and psychologic consultation. But a book of this type always presents the danger of tempting school teachers and other lay observers of "problem children" to make snapshot diagnoses, whether of physical or mental conditions, without basis in fact or training. Bisch does not wholly circumvent this danger. Photographs of patients labeled "precocious child," "psychoneurosis," "dementia precox," give the erroneous impression that such photographs are of value and that a diagnosis might actually be made from them. So far as the teacher learns to recognize a child as atypical for the purpose of referring him to the mental clinic or of advising expert study, the author's aim is laudable. If the teacher feels competent to diagnose epilepsy or congenital syphilis on the basis of Chapters XII and XIII (thirty-one pages) much harm may result. Besides containing errors, they are inadequate for the medical man and can be only confusing for the layman.

Chapter II presents a complete outline for history taking and examination — complete, though rather impracticable for clinical use. Much stress is placed on heredity. The term moral deviation in Chapter X is a cover-all for delinquent behavior of all types not remediable by current methods, and presents no advantage over older terms. The implication in the word "moral" moreover, is opposed to the medical attitude toward abnormal behavior. The book in general is not well balanced for teaching purposes. Only ten pages, for example, are devoted to "functional conditions" of childhood; yet there are twenty pages on epilepsy, with statistical lists of the numerous types of aurae and other such details that have a place only in special articles on the subject.

HYPNOSE: METHODIK DER ERZIELUNG DES HYNOTISCHEN SCHLAFES BEI MENSCHEN. AUGUST BOSTROEM. METHODIK DER VERSUCHE ÜBER TIERISCHE HYPNOSE; ERNST MANGOLD. Mit 18 Abbildungen im Text. From the Handbook of Biological Methods. Edited by Prof. Abderhalden. Price 3.30 marks. Pp. 87. Berlin: Urban & Schwarzenberg, 1925.

The chapter by Bostroem begins with a terse definition of hypnosis followed by a definition of suggestion which is satisfactory. The author then makes some very sensible remarks on the procedure of hypnotizing in the practice of medicine, even suggesting that the operator should make a careful toilet of the hands

so as to avoid "unfavorable impressions." The matter of susceptibility to hypnosis is also treated in a reasonable and practical way, likewise the possible dangers.

The varying degrees of hypnosis and its bodily effects are briefly covered, and the author then passes to the procedure itself — the technic. Here, too, he is sensible. Instead of recounting the manifold methods that have been and still are employed, he gives his own method (a good one) with sufficient explanations to enable one to vary it as the occasion and the patient seem to indicate. Degrees of success and difficulties are sufficiently noted, and the article closes with excellent advice and comments on many phases of hypnotism as a practical therapeutic agent.

The chapter by Mangold is of no practical value to physicians and has little medical interest, but any one may be interested in the hypnotic state (or at least something similar) induced in chickens, mammals, reptiles, amphibians and even fishes. The author begins with chickens because the induction of a state of akinesia in poultry was introduced as long ago as 1636 (Schwenter). Among mammals, guinea-pigs and rabbits are the most susceptible, but the method of inducing "hypnosis" in other animals as well as in the lower orders is described.

When we come to insects the condition is not so clear as it probably is closely related to the "possum playing" reflex (Totstell reflex — thanatosis) of many insects.

The chapter closes with an interesting discussion of the various factors influencing the susceptibility in lower animals and the effect of this akinesia on the organism.

TABULAE ANATOMO-COMPARATIVAE CEREBRI. A SERIES OF NINE COLORED MAPS WITH DESCRIPTION. Edited by C. U. ARIËNS KAPPERS, Director of the Central Institute for Brain Research. Price, $20.00. Amsterdam: The Kosmos Publishing Co., 1925.

These charts (about 80 by 110 cm.) are designed to aid students of the comparative anatomy of the brain to grasp the salient features of the internal structure and fiber connections of representatives of the chief vertebrate groups: *Amphioxus, Petromyzon, Scyllium, Periophthalmus* (a teleost), *Rana, Varanus, Gallus, Onychogale* (a marsupial), *Homo*. The chief nuclei and fiber tracts are colored according to a uniform plan in all, so that their modifications from type to type can readily be followed, and they are fully labeled. There is a brief descriptive text (thirty pages) in which attention is called to the chief characteristics of each type illustrated. Kappers' great work, "Die vergleichende Anatomie des Nervensystems," Haarlem, 1920-1921, may be used as a more complete descriptive text.